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THE DEFENSIVE MECHANISM OF THE PARAMETRIUM DURING PREGNANCY AND LABOR

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There are few subjects in obstetrics about which a greater volume of literature has accumulated than the pathology of puerperal infection. But, while all investigators agree in the view that the direct introduction of pyogenic bacteria into the genitalia by means of the hands or instruments represents the chief source of infection, the questions of auto-infection, as well as of nature's methods of protecting the puerperal woman, still remain open. A considerable amount of information is now available with regard to the presence of pyogenic bacteria in the vaginal secretion during pregnancy, which has been discussed vigorously for the last two decades. In general, it may be said that the laborious bacteriological researches have led to the conclusion that "the preponderance of evidence indicates that in a varying proportion of patients the vaginal secretion does contain streptococci" (Williams). The question was fully discussed at the recent meeting of the Fifth British Congress of Obstetrics and Gynecology in London, but, in spite of a great deal of careful study and investigation, there is yet much controversy and lack of accord as to whether bacteria which are harbored in the vagina and the cervical canal may or may not develop pathogenicity.

Turning to another side of the problem under consideration, our knowledge is very defective concerning the defensive forces which may be operative in coping with puerperal infection. Indeed, it may be said that the actual facts are limited to the occurrence of leucocytic infiltration,—the reacting zone beneath the infected area which confines the microorganisms to the inner surface of the uterus and thus prevents further invasion.

The present investigations were carried out, in the attempt to obtain information as to whether there exists in the tissues immediately involved in the resorption of bacteria during labor a mechanism

adapted to repelling their invasion. In considering the various factors which favor infection of the puerperal tissues, the presence of bacteria, the succulence and bruising of the tissues, and the occurrence of lacerations, it is apparent that the parametrium has received but little consideration, and it seems to us to call for particular attention. Accordingly, the question which presents itself, is whether or not there can be demonstrated, in the base of the broad ligaments during pregnancy and labor, any visible evidence of a histological reaction which can afford any basis for believing that it may assume the function of a protecting and defending apparatus, either continuously in operation or capable of responding upon immediate notice. If we take into account the paths by which bacteria may be absorbed from the surface of the slight or severe cervical lacerations, which occur in almost every labor, we may say that they travel through the cervical wall by way of the lymphatic vessels or the lymph spaces, as the lymphatics draining the upper part of the vagina and the cervix unite at the lateral margin of the cervix and, following the course of the vessels, pass into the dense connective tissue of the parametrium.

Since these lymphatics are often involved in carcinomatous disease of the cervix, and the parametrium is frequently invaded, much attention has been directed to the microscopic examination of this structure, and valuable contributions along such lines have been made by Kundrat, Kermauner, and Sampson. Among other important findings, the fact emerged from the careful studies of these writers that carcinoma cells are to be found at times in definite lymph vessels, but that more often they make their way along the lymph spaces of the parametrium. While numerous investigators have been engrossed in elucidating the finer details associated with the growth of carcinoma cells in the lymph spaces, no attention, strange to say, has been directed to the conditions obtaining in the parametrium during pregnancy and the puerperium, and careful search of the literature has failed to reveal a single reference to the subject.

MATERIAL AND METHOD

Since a proper understanding of the peculiarites of tissues under abnormal conditions cannot be obtained except on the basis of a

knowledge of the normal state of affairs, an exact picture of the parametrial activity during normal pregnancy and labor appeared to be the first consideration. Therefore, our attention was primarily directed to the study of the parametrium obtained from full term pregnant uteri which had been removed for the purpose of sterilizing the patient, that is to say, when repeated Caesarean section was followed by hysterectomy. Since in this service this procedure is carried out at an appointed time before the onset of labor, histologic examination will obviously reveal the normal condition of the tissues in question at the end of pregnancy. Further information was obtained from specimens removed after the labor pains had been in action for several hours, while uteri removed on account of pelvic dystocia, associated with ascending infection, offered a welcome opportunity for studying the conditions under the stress of labor on one hand, and under the influence of infection on the other. Furthermore, an investigation as to the essential occurrences during the preceding months of pregnancy turned out to be a necessary supplement to our studies as to the origin and development of certain types of cells.

With this in view, a series of 43 specimens was submitted to microscopic examination of the base of the broad ligament and the outer layers of the uterine wall. These were in part obtained from the collection of the obstetrical department and in part consisted of fresh specimens obtained at operation during the current year. In addition, several specimens obtained by the courtesy of the gynecological department afforded the material necessary for the study of the parametrium under normal, non-pregnant, conditions.

In the routine hardening and fixing of the specimens 10 per cent formalin was replaced in some instances by absolute alcohol to permit the employment of certain staining methods. Methyl-green pyronin served for differentiating "mast" and plasma cells, and Giemsa's solution for staining bacteria. McJunkin's benzidine method was used for staining granulocytes.

OBSERVATIONS

Upon studying the conditions obtaining in the parametrium during normal pregnancy and labor certain definite cellular reactions can

be noted, to which we believe attention has heretofore not been directed. Whereas in the non-pregnant woman the base of the broad ligament is built up of dense fibrillar connective tissue including but few cell elements and occasional bundles of plain muscle, at term and during labor throngs of well characterized cells make their appearance in this region. These cells are arranged in relation to the course of the lymphatics which accompany the uterine vessels, and can be sharply differentiated into two types. One group consists of cells, to which the name clasmatocyte or histiocyte has been applied; while the other group is represented by cells corresponding to the type of monocytes. When hemorrhage occurs into the parametrium, both groups of cells engulf red blood cells. In such circumstances, either well preserved erythrocytes or their fragments can be seen, which in most instances lie within the cytoplasm adjacent to the nucleus. In other places the cells contain particles of brown pigment. When fresh specimens are subjected to vital staining with neutral red, the majority of these cells exhibit granules which have taken up the dye. By the ready demonstration of this affinity for neutral red and of the ability to ingest red blood cells, clear cut anatomical data as to the phagocytic ability of these strains of cells have been adduced. To these two categories another type of cell must be added, which invariably constitutes a distinct feature of the cell strands mentioned. Close proximity to the smaller blood vessels and the presence of coarse granules in the cytoplasm are quite specific for this type of cell, which may be regarded as the stem-cell of mesenchymal origin from which the clasmatocytes and monocytes are derived.

The cellular reaction of the parametrium during pregnancy and labor can best be understood by describing the variable appearance of this region under different conditions. In order to avoid repetition, the following descriptions will give an idea of the characteristic changes in the parametrial district which go hand in hand with the advancement of pregnancy, the onset of labor and the occurrence of infection.

Group I. Uteri removed on account of prolonged labor; beginning infection

On inspection of the parametrium with the low power the most obvious change, as compared with the conditions in the non-pregnant stage, is the marked increase in the number of cells which have

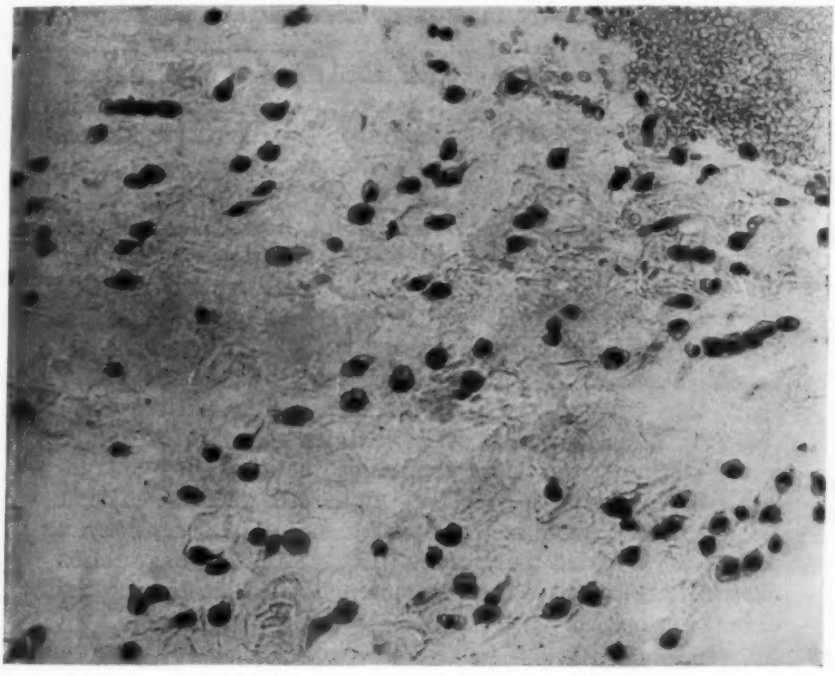

FIG. 1. PARAMETRIAL TISSUE FROM A UTERUS REMOVED AT CAESAREAN SECTION FROM A PATIENT PRESENTING SIGNS OF BEGINNING INFECTION, SHOWING AN INCREASE IN THE NUMBER OF CLASMATOCYTES AND MONOCYTES. × 300

invaded the connective tissue. Under higher magnification, it is seen that the cells occur in rows and lie between the tissue strands, in part forming groups of from three to five individuals. A good example of a specimen field is presented by the photomicrograph Fig. 1. One set of cells is almost uniform in size, 15 to 20 micra in

diameter. Their dark nuclei appear large in comparison with the amount of cytoplasm, and are either kidney-shaped or, less frequently, round with ragged outlines; they are surrounded by a lucid halo (monocytes). More numerous, however, are larger cells, 20 to 30 micra in diameter. Their nuclei occupy an eccentric position and are usually oval in shape, in some instances presenting an indentation, while the chromatin net-work is rather indistinct. A few binucleated cells are clearly seen. It is significant in this connection that a certain number of small round cells are found scattered between the large branched clasmatocytes. Since they exhibit distinct phagocytic activity, as shown by the intracellular inclusion of debris, and are identical with the clasmatocytes, in every histological detail, it is obvious that they are derived from the division of the larger forms. It is at once seen that the protoplasm of the clasmatocytes is much more conspicuous and that they present great variations in shape and dimension. Most of them are oval, rounded, pear-shaped, or quadrangular, while others are irregular in outline, with elongated processes at one or both poles. The cytoplasm presents a vacuolated appearance. At times this is limited to the inner layers only, but more frequently it extends throughout the entire cell. The vacuoles in the individual cells vary greatly in size; in the most instances several larger vacuoles can be seen, lying close together at one side of the cytoplasm. In the cells which are adjacent to areas where hemorrhage has occurred fragments of erythrocytes may be found within the vacuoles. In such places a brown blood pigment likewise makes its appearance, either within the vacuoles or in the cytoplasm.

Group II. Porro at repeated Caesarean section at term, several hours after the onset of labor, but no infection

The parametrium shows substantially a picture similar to that just described. Under high magnification (Fig. 2) a dense collection of macrophages can be seen, among which the clasmatocytes are quite conspicuous. They are, however, not nearly so numerous as in the preceding case, and both monocytes and clasmatocytes are present almost in the same proportion. A marked feature of this stage is the occurrence of mitotic figures, which can be seen chiefly

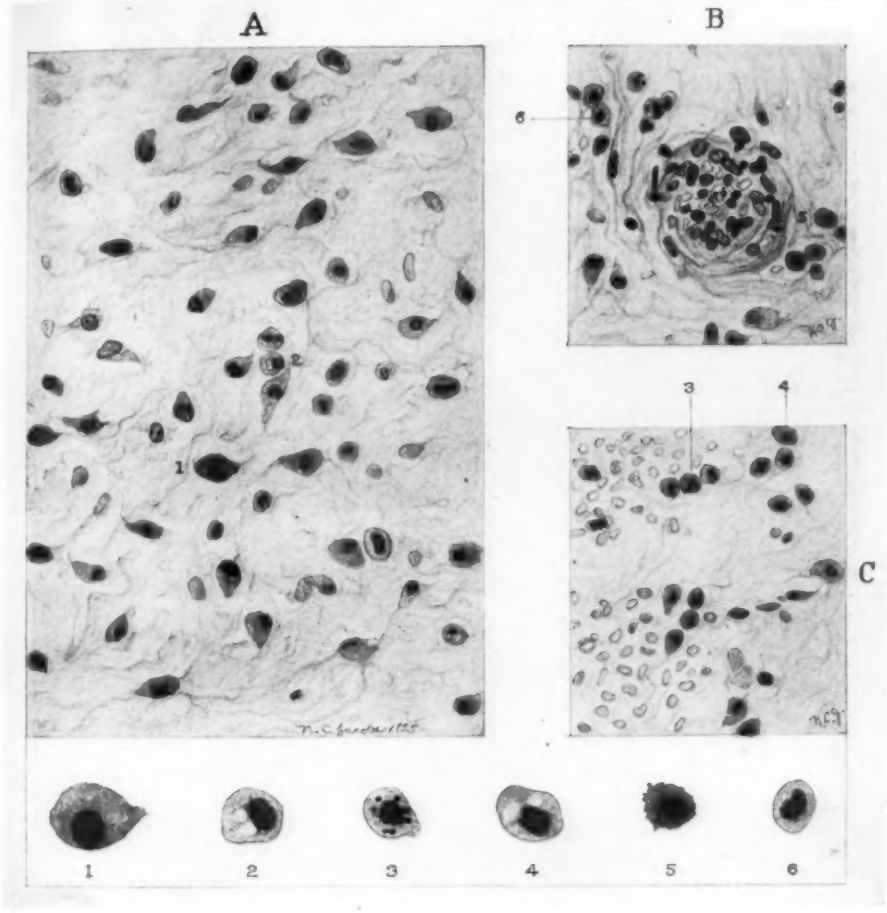

FIG. 2

A shows the characteristic structure of the phagocytic tissue at the onset of normal labor.
B shows the development of macrophages from the stem-cells in the vicinity of a small vessel.
C shows the presence of blood pigment in macrophages at the periphery of an area of hemorrhage.
1, *2*, *3* and *4* show various phenomena occurring in clasmatocytes; *5*, transitional stage between stem-cell and clasmatocyte, showing the presence of granules; *6*, monocyte (oil-immersion).

in the monocytes, and less frequently in the clasmatocytes. The benzidine method shows brown-colored granules in some of these macrophages. Furthermore, we have to note the presence of another type of cells, which lie in groups of 2 to 4 in the immediate neighborhood of the smaller blood-vessels. They are characterized by an accumulation in their cytoplasm of coarse granules, which take up eosin with avidity. As the granules do not stain so brightly as in the eosinophilic cells, the term pseudo-eosinophilic seems justifiable. Indeed, it is this peculiarity in coloration which brings these cells, which are much less numerous than the macrophages, into prominence. These cells are oval or round, measure 8 to 10 micra in diameter, and contain an oval smoothly outlined nucleus. They also occupy the interstices between the muscle bundles of the outer layers of the cervix. In some instances their cytoplasm becomes definitely enlarged, the coloration of the granules less bright or even indistinct; in other instances a halo appears in the periphery of the nucleus, and the outlines of the cells grow ragged and irregular. It is a striking feature that these transitional stages can be demonstrated all the way from the original cell to monocytes and clasmatocytes, so that it would appear that this type of cell, which was originally limited to the immediate vicinity of blood-vessels, is to be regarded as the stem-cell, which furnishes the recruits for the army of macrophages in the parametrium.

The findings in one specimen in this group deserve special attention. Several months ago we had to deal with a multipara, who had given birth spontaneously to a living child four hours previous to admission. After the placenta had separated, the attending physician found another child outside of the main uterine cavity, and sent the patient to the hospital. Here it was found that we had to deal with a bicornuate uterus which had been pregnant in both horns, and it was decided to remove the entire structure by hysterectomy, in order to prevent the spread of infection. This specimen offered an extraordinary opportunity for studying the conditions of the parametrium in the same individual, when delivery had been effected on one side but not on the other. It was found that the development of the phagocytic tissue was much less pronounced on the undelivered side.

Furthermore, I wish to emphasize the important point, that in this, as well as in the first group, the occurrence of phagocytic cells is decidedly less abundant in the loose connective tissue, which constitutes the upper part of the broad ligament, than at its base.

Group III. Hysterectomy following Caesarean section at an appointed time before the onset of labor

A local excess of macrophages is still evident, though less conspicuous than in the two foregoing groups. The monocytes prevail. The cytoplasm of the cells is either homogenous or vacuolated in part, but a foam-like appearance is very rarely noted. The original stem-cells are quite abundant and present the same features as described above. Methyl-green pyronin fails to stain their granules. We likewise frequently encounter the transitional type of cell which was described in the preceding group. From their appearance it will be at once inferred that a hypertrophy of the cytoplasm of the original cell has taken place, and that coincident with this hypertrophy and a loss of granules, the cells have become quite similar to macrophages. The original stem-cell, however, does not display any evidence of phagocytosis. The occurrence of plasma cells could be noted in a few instances. Finally, the progressive enlargement of the spindle-shaped connective tissue elements is noteworthy. Their cytoplasm appears broader and thicker so that the cells resemble fibroblasts. With this hypertrophy there is associated an acquisition of some phagocytic power, as is evidenced in a number of instances by the ability to store blood pigment. But this ability nowhere attains the same intensity as in the adjacent macrophages. It is very striking that in studying these conditions in our various specimens, one is impressed by the obvious differences in the degree to which this fibroblast-like tissue has developed.

Group IV. Third month pregnant uteri

We may summarize the findings within the parametrial tissue at this stage of pregnancy by saying that in comparison with the non-pregnant state there is an evident increase in number of the original cells. In part they are still lying in close proximity to the small

vessels in groups of two to four; in part, however, they are distributed between the tissue fibres. But with reference to their relative quantity, there is a noticeable difference in the various places. Closer study reveals the presence of transitional forms, and in some in-

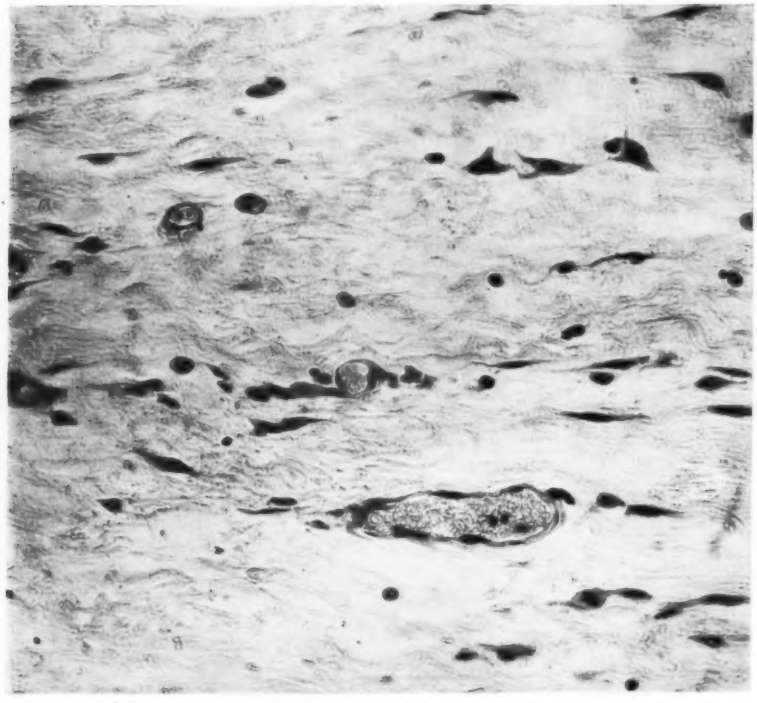

FIG. 3. EARLY STAGE IN THE DEVELOPMENT OF PHAGOCYTIC TISSUE AT THIRD MONTH OF PREGNANCY

Note the strand-like arrangement of the cells, and their relation to blood vessels. × 300.

stances the first phenomenon observed is that the cytoplasm grows more voluminous, and at the same time the outlines of the cells become ragged or irregular as the result of the formation of protruding processes. Here and there vacuoles make their appearance,

while mitosis occurs rather infrequently. The microphotogram (Fig. 3) shows these conditions.

Group V. Uteri six months pregnant removed on account of various indications

In comparison with the foregoing group, there is a perceptible increase of the original cells in the parametrium, as well as in the broader strands of connective tissue in the outer layers of the cervix.

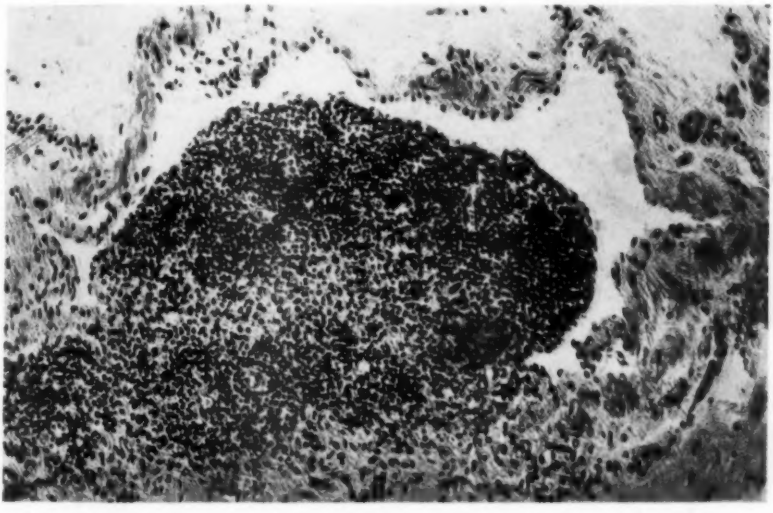

FIG. 4. DEVELOPMENT OF A LYMPH NODE IN THE WALL OF A PARAMETRIAL LYMPH VESSEL. × 140

Lying in groups of five or six, they present all the transitional stages leading to the formation of monocytes and clasmatocytes. The cytoplasm of these cells is still rather inconspicuous. Their nuclei become kidney-shaped, sometimes surrounded by small vacuoles. Mitotic figures occur decidedly more often than in the earlier months. As to the specific spindle-shaped elements of the connective tissue, it is noteworthy that by their swelling these cells appear broader and longer; and that this transformation brings the whole structure more into prominence.

Besides the cellular reaction occurring in the vicinity of the lymphatics which make their way through the parametrium, there is another interesting phenomenon which in several instances could be observed within the walls of larger lymph-vessels. In such circumstances cells of adenoid or lymphoid character, which in the non-

FIG. 5. CROSS-SECTION THROUGH AN INFECTED CERVIX, SHOWING LEUCOCYTES AND PHAGOCYTIC CELLS. × 300

At *a* is seen a red blood cell engulfed in a clasmatocyte

pregnant state are now and then seen in closest proximity to lymphatics of the parametrium, undergo marked proliferation, with the result that miniature lymph glands develop beneath the endothelium, and project into the lumen of the vessels, forming plateau-like structures, as shown in Fig. 4. It seems quite probable that this formation of lymphoid tissue may play the same biological rôle

as the ordinary lymph nodules of the parametrium. Moreover, the fact that similar formations are frequently noted in the development of lymph-nodules during embryonic life suggests the possibility that their sudden development during the latter part of pregnancy may be associated with some specific function.

In the cervical tissue itself, the intense acute inflammatory reaction resulting from intra-partum infection, which extends outward into the muscularis through the lymphatics, is characterized in the majority of cases by an abundant leukocytic infiltration. On the other hand in two cases in our series clasmatocytes take part, to a remarkable degree, in the formation of the accumulation of cells in the connective-tissue spaces between the muscle bundles. (See microphotogram Fig. 5.) It must, however, be mentioned that there is no continuity to be noted between these strands of cells and the phagocytic tissue in the parametrium. That is to say, the formation of the cell groups within the cervical and the parametrial tissue does not appear to be correlated. In both cases streptococci and bacilli were cultivated. Since this peculiar reaction of the cervical tissue was noted but twice, it would be hazardous to discuss whether it was in any way associated with the satisfactory outcome in both patients.

DISCUSSION

The histological conditions obtaining in the parametrium during pregnancy and labor have been studied in this paper in the hope of learning something of the nature and significance of the biological processes occurring in this tissue in association with the various physiological states of pregnancy, and the possibility of their playing some part in increasing the resistance of the patient to infection. From our studies of the conditions obtaining in this region it is obvious that several phenomena must be considered, the most notable being a remarkable development of phagocytic tissue within the tissue spaces of the base of the broad ligament, which is particularly accentuated under the stress of prolonged labor—a period which presents the high-water mark of macrophage activity.

The immediate impulse to our investigations was furnished by the current conception that local tissue immunity constitutes one of the

most important medical problems. There is an increasing impression that even the temporary limitation of an infection resulting from the invasion of bacteria may determine the eventual outcome, and further, that local reaction at the portal of entry tends to prevent general involvement. Local resistance in various organs is attributable to the phagocytic action of macrophages, and there are abundant indications pointing to the active rôle which this cell type plays in defensive processes, not only against chronic infection, but also against acute phenomena as well.

Up to the present, our knowledge of the behavior of the broad ligament in the presence of infection is practically limited to the gross anatomical changes developing in parametritis and broad-ligament abscess, but insufficient attention has been devoted to its histological features, and particularly to the mechanism by which it is enabled to resist infection. In this connection, after having finished the present study it was very interesting to learn that many of those discussing the reports on puerperal infection at the Fifth British Congress of Obstetrics and Gynecology laid the greatest stress upon immunities provided by nature for overcoming the effects of infection by pathogenic bacteria during labor. It was emphasized that "Useful as research into the kind of sepsis may be, research into the causes of resistance in pregnant and puerperal women is likely to be more fruitful in results" (page 252), and again "We must study the pregnant woman more carefully than we have done,—we have to consider what her condition actually is" (page 249). It is particularly in this respect that our investigations may be of service, in so far as they fill in part this lack in our knowledge. At the same time, I do not wish to be understood as minimizing the part which may be played by the immune bodies that may be present in the blood in influencing the resistance of the individual to general infection; although phagocytosis is recognized to be the usual and perhaps inevitable expression of the destruction of bacteria.

Our investigations clearly show that the response of the parametrium to the development of pregnancy is very striking. We have shown that at term some of the large macrophages of the parametrium are marshalled from the ranks of the resting-wandering cells, which are always present in this tissue, and may be presumed to

travel to the place of danger in response to a call to arms, and that the great majority of these cells develop from the small oval cells adjacent to the vessels, giving rise to the free mononuclear phagocytes. There is considerable evidence that the monocytes, as well as the clasmatocytes, within the parametrial tissue during pregnancy, develop *in situ*, and that the primitive cell in the vicinity of the blood vessels, identical with Marchand's adventitial cell, is to be regarded as their "stem-cell." From the third month of pregnancy on, we can readily trace all stages of their development and maturation, and can see the cytoplasm become more voluminous until it gradually takes on the appearance of typical monocytes and clasmatocytes. A similar metamorphosis likewise occurs in the acquisition of a high phagocytic power; with the result that the essential representatives of the tissue, although derived from cells of diverse morphological type, come to resemble one another closely.

Although, in general, no final decision as to the origin of clasmatocytes and monocytes has been reached by histologists, all who have investigated the subject agree that there is a close biological relationship between the two types of cells. A recent study of the question by Cunningham, Sabin and Doan, points to the view that under conditions of irritation the monocytes may arise locally from primitive cells. By their remarkable power of cell division monocytes may ultimately outnumber the clasmatocytes in an irritated area; but, on the other hand, clasmatocytes, being a highly phagocytic type of cell, react with greater readiness in taking up debris and bacteria. In our studies the phagocytosis of red blood cells both by clasmatocytes and monocytes, and the storage of blood pigment within the cytoplasm of these cells, could be demonstrated. Moreover, the staining of the cells by neutral red indicates their ability to phagocytize cellular debris, bacteria and other particulate matter, in accordance with the view that phagocytic power runs parallel to the staining by vital dyes.

Furthermore, it has been shown by Widal, Nakahara, Gay and Morrison, and others, that under various experimental conditions, coincident with the marked reaction of macrophages, there is an increased resistance to bacterial infection. Likewise, there is accumulated evidence that macrophages concerned with the

removal of debris play an important rôle in the healing of bone-wounds (Macklin), in the localization of infection within the subarachnoid space (Essick), as well as in the omentum (Cunningham). Hornung, in studying infected uteri, demonstrated the presence of large mononuclear cells in the decidua beneath the infected area, and showed that in many instances they extended for some distance into the connective-tissue spaces between the muscle fibers, and drew the conclusion that the cells in question play an important part in localizing the infection.

What is the influence, it may be asked, which during pregnancy causes the development in the parametrium of a phagocytic tissue, which is evidently intensified under the stress of labor? Since for the last few years pathologists emphasize that due to irritation by foreign protein substances in various organs there is a response of mesenchymal tissue elements and of undifferentiated cells in the immediate vicinity of blood vessels, our attention was first of all directed to a causative factor of this kind. There is, however, nothing which leads us to believe that the specific stimulant in the parametrium is the result of the breakdown of foetal or chorionic tissue. It is unlikely that the well known proliferation and breaking off of buds of chorionic tissue into the maternal blood-stream—the so-called deportation—can be considered the main factor; particularly as this is most marked in the early stages of pregnancy, while the parametrial changes attain their highest development at its very end. On the other hand, it is conceivable that the hormone or whatever substance it is that produces the well known changes in various organ of the pregnant woman, causes the parametrial phenomena. In regard to the conditions obtaining during pregnancy in the larynx, the lungs, the bladder and so forth,—closely resembling subacute inflammation—the reader is referred to my monograph "Changes of the Maternal Organs during Pregnancy."

In view of the conflicting statements concerning the presence of pathogenic bacteria in the vaginal secretion of normal women at the end of pregnancy, it would seem inadvisable to consider the part which they might play if their presence is eventually demonstrated. On the other hand, in the presence of actual infection at the time of labor, it is altogether likely that the bacteria which gain access to

the parametrial tissue through smaller or larger cervical tears would give rise to the irritation necessary to stimulate proliferation of the phagocytic tissue, which in all probability would lead to the local limitation of the infectious process, provided the offending bacteria were not of excessive virulence. In other words, the activity of the parametrial tissue in question must be regarded as a most beneficent mechanism in the production of local immunity.

In order to give a complete picture of the defensive forces of the parametrium we had for consideration the lymphoid tissue within the wall of lymph-vessels. As shown in Fig. 4, with pregnancy there is correlated a marked hypertrophy of these nodules, causing them to be protruded plateau-like into the lumen of the vessels. It is noteworthy that similar observations have been made by Kundrat and Sampson on parametria obtained at operations on account of carcinoma of the cervix.

The question as to whether a stimulation of the cellular reaction of the parametrium by therapeutic measures may or may not be effective in the treatment of puerperal infection, lies beyond the scope of this paper. The participation of macrophages in the formation of v. Rosthorn's lateral horizontal exudates located in the base of the broad ligament following infection in puerperal and gynecological cases likewise offers a subject for further research.

In conclusion, I would not omit to emphasize that in studying the conditions of the lower uterine segment in infected cases there is positive evidence that throngs of macrophages beneath the peritoneal covering can be seen. But I do not commit myself to any opinion as to whether their protective service proves to be of additional value in justifying low cervical section in cases suspicious of being infected.

CONCLUSIONS

During pregnancy a phagocytic tissue, consisting of monocytes and clasmatocytes, makes its appearance in the base of the broad ligament, and is intensified under the stress of prolonged labor but particularly by the existence of infection. The development of this tissue from resting-wandering cells and adventitial cells can be demonstrated.

The presence of this phagocytic tissue in the parametrium must be regarded as a prophylactic biological reaction and as a marked protection against infection. It certainly affords a mechanism for the development of local immunity in a region abundantly predisposed to infection, and must be of service in doing away with debris and bacteria.

The mode of its production is not yet clear, but it may have important implications in connection with the questions of auto-infection and low cervical section.

The development of lymphoid tissue within the walls of lymphatics in the parametrium must be regarded as an additional defensive mechanism.

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THE SYMPTOMS OF CORONARY OCCLUSION

LOUIS HAMMAN

From the Medical Clinic of the Johns Hopkins Hospital and University

INTRODUCTION

One is surprised in reviewing the literature of coronary occlusion to find no systematic account, dating from more than fifteen years ago, of the clinical symptoms accompanying this grave accident. This omission is remarkable because the symptoms are dramatic and arrest attention and the anatomical lesions are gross and obvious in their implications. It is unbelievable that astute physicians could have failed to observe the symptoms or to draw correct inferences from the lesions. As a matter of fact they did not fail in either respect. It would be an error to represent the symptoms of coronary occlusion as a modern discovery, for the medical literature of the past century and a half is crowded with clinical and pathological observations upon the condition. Huchard, to fortify his contention that disease of the coronary arteries is the necessary anatomical basis of angina pectoris, diligently collected the records of 185 autopsies upon the bodies of patients who had died of this disease. If you will read over these records, even in the condensed form in which Huchard reports them, you will be able to cull out all the essential clinical and pathological features of coronary occlusion. You will find there described the status anginosus, the symptoms of myocardial insufficiency following the attack of pain, the pericarditis and the pericardial friction rub, the feeble cardiac impulse and distant heart sounds, the pulmonary edema, pulmonary infarction and other embolic phenomena, the cardiac infarction, cardiac scars and aneurysm, the sudden death, delayed death and even recovery from the accident. No less clearly stated and somewhat more perspicuously interpreted we find many of these same symptoms in Krehl's monograph upon disease of the heart muscle. He describes clearly the formation of cardiac infarcts and the subsequent scar formation and discusses their effect upon myocar-

dial efficiency. The lack of any constant relation between the extent of scarring and the degree of functional disturbance leads him to surmise that the location of the damage is an important factor in determining the occurrence of disorder of function. He comments upon the fact that occlusion of a large branch of the coronary artery, for example, the anterior descending branch, may go unmarked by any conspicuous symptoms, and yet autopsy years later may reveal an old calcified infarct. In other instances the accident may be accompanied by intense stenocardia and the onset of severe myocardial insufficiency. Death may follow instantly or hours or days later, or the patient may recover and the gravity of the peril through which he has lived be disclosed only years later when at autopsy a large healed infarct is found. He notes that these scars sometimes give rise to aneurysms which may finally rupture and cause sudden death. Furthermore, he discusses the great variation in symptoms following coronary occlusion and points out that the symptoms are likely to be mild when there is diffuse sclerosis of the vessels and that they are likely to be severe when the vessels are relatively healthy and the occlusion occurs suddenly. Finally, he confesses to mystification at the remarkable suddenness with which death often comes. This is not like the death of circulatory failure. He is convinced that under these circumstances something extraordinary goes on in the heart which has not been satisfactorily explained.

However, we need not go so far abroad to seek evidence of the familiarity of diagnosticians with the symptoms of coronary occlusion during the latter half of the past century. Many physicians practising today will remember pertinent observations and comments made by their teachers. Most of these, if published at all, are recorded under the heading of angina pectoris. Dock in 1896 reports a number of interesting examples in an article entitled "Some Notes on the Coronary Arteries." Osler has unmistakable instances in his monograph on Angina published in 1897, and he amplifies and adds to these observations in his Lumleian Lectures in 1910.

In view of the fact that there were such extensive pathological data upon coronary occlusion and so many observations upon the symptoms accompanying the accident before the close of the last century, I repeat, that it is surprising not to be able to find a comprehensive and

systematic account of these clinical symptoms earlier than fifteen years ago. Even today one will search in vain for such an account through the various textbooks and systems of medicine and will find only a brief and unsatisfactory statement in special monographs dealing otherwise exhaustively with disease of the heart. The reason for this omission must reside in some peculiar way of viewing the matter, and this peculiarity, I believe, is no other than the complete mental fusion that has existed between coronary disease and angina pectoris. Coronary occlusion has been considered an episode in the progress of angina pectoris, a harrowing episode it is true, and yet but the dramatic ending of an interesting and varied clinical story. Medical authors long neglected to place it in bold relief as an independent clinical condition and therefore failed to note carefully and in detail all of its characteristic features and to draw so clear and definite a picture that any physician familiar with its outlines might recognize it almost at a glance. All of the older observations on coronary occlusion are buried beneath discussions of angina pectoris and so late as two years ago an eminent clinician revealed some of the most interesting observations upon coronary occlusion under the title "Reflections upon Angina Pectoris."

Although there is, then, nothing novel to the symptoms of coronary occlusion, still during the past decade and a half they have been collected and connotated in an altogether novel way. The diagnosis of coronary occlusion was seldom ventured ten years ago and prior to fifteen years ago it was almost unheard of except as an explanation of sudden death in angina. Today the diagnosis is being made with increasing ease and frequency, and as the profession becomes better acquainted with the characteristic features of the accident, it will become a familiar clinical condition. Then, too, will disappear much of the terror with which the accident is clothed, for it will be found that as many patients recover, at least temporarily, as immediately succumb to it. It is important for physicians to be familiar with the condition, for diagnosis has something more than academic interest, since prompt recognition of the accident may promote recovery.

HISTORICAL NOTE

The first satisfactory account of the symptoms of coronary occlusion was published by two Russian physicians, Obratzow and Stra-

chesko, in 1910. These authors report three cases and express satisfaction at having predicted in two the diagnosis that was verified at autopsy. They comment upon the fact that they are able to find only one or two records in the literature of the diagnosis being correctly made, although, they add, there could have been no difficulty in recognizing the condition in two of their patients. They emphasize especially three points characteristic of the attack—the severe, prolonged pain, the *status anginosus*; the extreme dyspnea and orthopnea, the *status dyspnoeicus*; and the severe epigastric pain, the *status gastralgicus*. They speak in detail of the symptoms of myocardial weakness, *myopragia cordis*, and point to the evidence of feeble cardiac impulse and faint cardiac sounds. In the following year Hochhaus reports four cases with comments upon the symptoms. The first two cases that came under his observation he failed to diagnose because he was not familiar with the clinical picture. The second two he recognized at once, having in the meantime noticed the article of Obratzow and Strachesko. He summarizes his discussion by pointing out that the cardinal manifestations of coronary occlusion are the well known symptoms of angina pectoris in their most severe and extended form, accompanied by the signs of sudden and ever increasing heart weakness. In 1912 Herrick published his noteworthy article, the first of an important series of contributions from American clinicians. He deserves credit particularly for having emphasized more clearly than had been done before that occlusion of even a large branch of the coronary artery need not cause sudden death, indeed that death may be postponed for weeks and that not infrequently recovery takes place. From the clinical standpoint he divides instances of coronary occlusion into four groups: first, cases in which death is sudden, seemingly instantaneous; second, cases in which the attack is anginal, the pain severe, the shock profound and death follows in a few minutes or several minutes at the most; third, non-fatal cases with mild symptoms, difficult and often impossible to recognize; fourth, cases in which the symptoms are severe, are distinctive enough to be recognized, in which the accident is usually fatal but not immediately and not necessarily so. He gives particular attention to the last group.

Herrick's article stimulated the interest of American physicians in the clinical symptoms of coronary occlusion, but this interest was

not immediately productive of unusual literary activity and it is only within the past five years that contributions by Libman, Levine and Tranter, Smith, Gorham, Pardee, Paullin, Willius, Robinson and Herrmann, Longcope, Thayer, Wearn, Gordinier, Faulkner, Marble and White, and others have enriched our knowledge with such a wealth of detail that we may now draw a definitive clinical picture.

ANATOMICAL CONSIDERATIONS

It is not my purpose to comment in detail upon the anatomy of the coronary circulation. Had I the desire to do so, my labor would be rendered supererogatory by the excellent monograph of Gross. This investigator has diligently and painstakingly collected the voluminous literature pertinent to the subject and has added important original observations of his own. We may now speak simply of the facts of the coronary circulation since the time-honored dispute about the coronary endings, that is, whether they be terminal or freely anastomosing, has been satisfactorily settled. Some of these facts it is necessary to know before one can clearly understand the clinical symptoms of coronary occlusion and therefore preparatory to considering these symptoms, the relevant facts are recalled.[1]

The right coronary artery arises from the aorta a little below the level of the right anterior aortic cusp. It emerges upon the anterior surface of the heart between the roots of the aorta and pulmonary arteries and, lying in the auriculo-ventricular sulcus, half-way encircles the heart. At the crux the large ramus descendens posterior is given off and the reduced vessel terminates in two or three branches which descend on the posterior surface of the left ventricle.

The left coronary artery arises from the left anterior sinus of Valsalva just a little below the level of the free edge of the corresponding aortic cusp. After piercing the aortic wall it divides, under cover of the left auricular appendage, into the ramus descendens anterior sinister and the ramus circumflexus sinister. The former branch descends along the anterior interventricular furrow, rounds the apex

[1] The anatomical description follows Gross very closely. Some phrases and an occasional sentence are copied verbatim. This acknowledgment makes the use of quotation marks unnecessary.

and ascends the posterior interventricular furrow to reach the lower third of the ventricles. Along its course it gives off numerous branches to the right and left ventricles. The latter branch lies in the auriculoventricular sulcus and half way encircles the heart to end in numerous branches upon the posterior surface of the left ventricle.

The right coronary artery supplies the entire right ventricle with the exception of the left third of the anterior wall. Its rami ventriculares sinistri supply the right half of the posterior wall of the left ventricle and a small strip of the interventricular septum.

The left coronary artery supplies the whole remaining part of the left ventricle, the left anterior portion of the right ventricle not supplied by the right and a small anterior strip of the interventricular septum.

The remaining portion of the septum and the papillary muscles receive their blood supply through branches derived from both right and left coronary arteries.

Besides the large branches which supply the heart muscle numerous small vascular twigs arise from both coronary vessels which are distributed to the epicardial fat—arteriae telae adiposae. They are seen in greatest number in the fat found under the epicardium, namely, in the grooves between the chambers, where they occur as an irregular network, and over the sites of the main coronary branches, where they occur as delicate parallel accompanying vessels. The rich interanastomosing network of delicate vessels superposed upon the outer coats of the root of the aorta and of the pulmonary artery falls under this same category. These vessels are of the greatest importance in determining the symptoms following coronary occlusion, because they form an extensive bed of anastomosing vessels which increase in importance with advancing years.

From the description given it is apparent that while the right coronary artery supplies chiefly the right ventricle it supplies also a portion of the left ventricle and, although the left coronary supplies chiefly the left ventricle, it likewise supplies an important part of the right ventricle. The anterior descending branch of the left coronary artery is of special clinical interest because it is more frequently occluded than are all other branches of the coronary arteries added together. I should estimate that in four-fifths of the instances of

coronary occlusion the anterior descending branch is the vessel involved. This vessel supplies the apex of the left ventricle, the left anterior third of the right ventricle and a portion of the interventricular septum. When occluded, the resulting infarct, if infarction occurs, will involve both the right and the left ventricle. These facts are pointed out because now and again the attempt is made clinically to distinguish occlusion of a branch of the right coronary artery from occlusion of a branch of the left. For instance, it is suggested that the occurrence of pulmonary embolism points to occlusion of a branch of the right coronary artery, whereas embolism to the brain, cord, viscera or extremities points to occlusion of a branch of the left coronary artery. A consideration of the true distribution of the coronary vessels will show at once how impossible it is to draw such a distinction from these symptoms.

The coronary vessels are subject to wide variation in their distribution. Gross analyzes these variations in detail. Some of them may influence the development of symptoms following occlusion. Two of these variations may be cited as examples. Occasionally, but a single coronary artery arises from the aorta instead of two and again, occasionally, there may be more than two openings. Still more frequently the right coronary artery is of relatively small size and ends at the margo acutus, the large posterior descending branch then coming from the left coronary artery. It is unnecessary to comment upon the clinical significance of these variations.

It has already been pointed out that an important source of difficulty in the way to a clear understanding of the symptoms of coronary occlusion is the great variation in the symptoms that follow apparently similar accidents. To mark the extremes, it is sufficient to note that the same accident may in one instance be followed, or rather accompanied, by instant death, whereas in another it may pass unnoticed and only later be accidentally discovered. Some explanation for these differences may be confidently advanced, but the full explanation is still awaited. There can be no doubt, as Krehl and many others have suggested, that the location of the injury to the heart muscle is a matter of eminent importance. Sudden death in experimental coronary occlusion is always accompanied by ventricular fibrillation and there is convincing evidence that under similar circumstances this

same abnormal mechanism often develops in man. It may even be suggested that it is the development of ventricular fibrillation which gives to sudden death in coronary occlusion its remarkable instantaneity.[2] Another puzzling clinical manifestation is the uneven manner in which cardiac arrhythmias appear, some patients hurrying on to death with a constantly regular pulse, while others progress uninterruptedly to recovery, exhibiting on the way various forms of irregularity. Interest at once fastens upon the conducting system of the heart in an effort to explain some of these vagaries, and the blood supply to this system becomes of paramount importance. As yet, however, the information gathered does not account satisfactorily for these clinical variations. Apparently, there is a distinct and specific blood supply to the sino-auricular and auriculo-ventricular nodes, and to the main bundle, the first part of the left limb and a large part of the right limb of the neuromuscular system. The sino-auricular node is supplied through a branch from the right coronary in about 60 per cent of the hearts studied by Gross; the auriculo-ventriculas node from the right in 92 per cent. The right limb of the bundle is usually supplied from the left coronary, the left limb by branches from both right and left. The remaining portion is nourished by vessels that supply the heart muscle upon which it rests. Observations upon alterations in the blood supply to the conducting system, as for instance those of Mönckeberg, refer chiefly to impaired function of the main bundle, namely, to heart block. It is well known that the conducting tissue at times shares pathological processes with the rest of the heart muscle; that at times it escapes; and, at times, is the sole part affected in generalized vascular disturbances. Since infarction following coronary occlusion affects particularly the internal surface of the heart, one might reasonably anticipate disturbance of function in the ultimate ramifications of the conducting system. However, these are protected by a very rich subendocardial network of anastomosing vessels, and even when extensive infarction has included Purkinje fibres in the area of destruction, the vast interlacing of the neuromuscular system may prevent the occurrence of any appreciable symptoms. It is possible that a careful comparison between the facts

[2] This matter was fully discussed by Dr. F. T. Fulton in a paper presented before the Association of American Physicians, May, 1925.

clinically observed and the results of detailed study of the cardiac lesion may finally elucidate the problem.

It is now universally accepted that there are abundant anastomoses between the right and left coronary arteries both in their capillary and precapillary distribution; that there is a rich anastomosis between the branches of each artery; and that anastomoses exist between the branches of the coronary arteries and vessels from the adjacent and attached organs. Although anastomoses in the heart are universal and abundant, still under ordinary circumstances they are not sufficiently extensive to prevent the formation of an infarct when a large vessel is blocked. However, the influence of a collateral circulation is plainly visible, since the infarct is always smaller than the area of heart muscle supplied by the occluded vessel. This collateral circulation is capable of wide development, and if a vessel be slowly and gradually narrowed, it may finally close and the heart muscle originally supplied by it remain fully and adequately nourished. Not infrequently, when one of the main coronary branches is found occluded at autopsy, a review of careful clinical records fails to reveal any symptoms pertinent to the closure, and a study of the heart fails to disclose the myocardial damage that might be anticipated. Gross reproduces the picture of the heart taken from a woman who had died of cancer of the gall-bladder at seventy-three years of age. During life there had never been symptoms of heart trouble and examination had failed to detect any evidence of cardiac disease. Yet at autopsy the right coronary artery was found extensively sclerosed and in several places almost totally obliterated. The myocardium was intact, there being no evidence of infarct, either recent or old. The beautiful photograph of the injected heart shows the most extensive anastomoses and illustrates particularly the conspicuous part played by the rami telae adiposae.

Gross calls attention to the remarkable fact that anastomoses throughout the coronary circulation become more extensive and more effective with advancing years. Other factors being equal, the heart of a man at sixty years of age is better prepared to withstand the effects of coronary occlusion than the heart of a man at twenty. Therefore, the extent of infarction that follows coronary occlusion depends upon many factors; upon the size and location of the vessel

occluded; upon the rapidity with which occlusion occurs; upon the condition of the general circulation and of the coronary circulation; upon the age of the patient.

EXPERIMENTAL CORONARY OCCLUSION

It is sufficiently clear from the preceding anatomical considerations that abrupt closure of a large vessel in a healthy coronary system will not exactly reproduce the symptoms that follow occlusion when the system is altered by disease. However, there is at least a gross resemblance between the two and certain experimental facts may be profitably compared with clinical observations. One not familiar with these experimental data will be surprised to learn that large branches of the coronary arteries may be tied with impunity and the animals live on apparently unaffected by the trauma. It is needless to review the long list of these experiments, beginning with the fatal attempts made by Chirac in 1698 and embracing the recent highly successful operations of Smith. Two of the most brilliant investigations are selected to illustrate the results obtained by modern operative technique. Miller and Matthews were able to ligate either main trunk of the left coronary artery without seriously disturbing the heart. Ligation of both branches always caused cardiac standstill. When either of the two main branches of the descendens was ligated, no evidence of cardiac disturbance was apparent for from one to three months. At the end of this time very acute symptoms of myocardial insufficiency often developed and rapidly proved fatal. They found that the previous administration of strophanthin allowed more extensive ligation of the coronaries without serious consequences. The results of Smith are comparable to those of Miller and Matthews. His list of operations is larger. The ramus descendens anterior sinister was ligated in eleven dogs:

1 died within two minutes after ligation with ventricular fibrillation.
10 survived the operaton:
1 died of sepsis.
1 died on the seventeenth day of myocardial failure.
1 was found dead on the eighteenth day
7 remained in good condition until sacrificed, 18 to 63 days after operation.

The ramus circumflexus sinister was ligated in fourteen dogs:

4 died during operation
4 died within 24 hours.
6 lived until sacrificed.

The right coronary was ligated in 8 dogs:

4 died within five hours.
1 died on the third day of sepsis.
2 were killed on the tenth and twentieth day, respectively; both had bronchopneumonia.
1 was killed on the twenty-eighth day, in good condition.

The ramus descendens anterior sinister and one or more branches of the ramus circumflexus sinister were tied in 18 dogs:

9 died within 24 hours.
3 died from infection on the third, twelfth and twenty-first day, respectively.
2 grew thin and died from failing heart on the fifteenth and seventeenth days, respectively.
4 were sacrificed from 42 to 89 days after operation.

The first lateral branch of the ramus descendens anterior sinister and one or more branches of the ramus circumflexus sinister were tied in 16 dogs:

6 died within twelve hours.
2 died from infection on the second and tenth days, respectively.
8 remained in good condition.

THE SYMPTOMS OF CORONARY OCCLUSION

The symptoms of coronary occlusion to be described are the symptoms that develop when a relatively large branch of the coronary arteries is obstructed and the obstruction is followed by the development of an infarct. It has already been pointed out that a large branch, indeed one of the main branches, of the coronary arteries, may be shut off so gradually that no symptoms mark the final complete closure. On the other hand, the occlusion of very small coronary branches produces symptoms only when a large number have been plugged. Under such circumstances myocardial insufficiency may gradually develop as a result of myocardial degeneration and fibrosis.

The condition is commonly described as chronic fibrous myocarditis. Wearn has pointed out that the classical symptoms of coronary occlusion do not occur when the occlusion comes on in the presence of myocardial insufficiency. There is then merely an increase of the dyspnea and cyanosis already present, and often only the suddenness of the change may suggest the real cause of the aggravation. This is an important fact to bear in mind and it will be recalled in discussing the symptoms of coronary occlusion. To facilitate description the symptoms may be conveniently divided as follows:

1. The immediate symptoms associated with the occlusion; the anginal seizure
   - A. Pain
   - B. Shock:
     1. Prostration
     2. Fall in blood pressure
     3. Suppression of urine
2. The symptoms associated with the myocardial damage, myocardial insufficiency
   - A. Dyspnea
   - B. Passive congestion:
     1. Cyanosis
     2. Pulmonary edema
     3. Enlarged liver
     4. Albuminuria
     5. Subcutaneous edema
   - C. Cheyne-Stokes breathing
   - D. Feeble cardiac impulse, faint heart sounds, gallop rhythm, murmurs, cardiac arrhythmias
3. The symptoms associated with the myocardial infarct
   - A. Fever and leucocytosis
   - B. Pericarditis
   - C. Embolic phenomena
   - D. Cardiac aneurysm and rupture
4. Additional symptoms
   - A. Nausea, vomiting, diarrhea
   - B. Facies
   - C. Vasomotor symptoms
   - D. Nervous symptoms

1. THE IMMEDIATE SYMPTOMS ASSOCIATED WITH THE OCCLUSION

The characteristic feature of the symptoms of coronary occlusion is their sudden onset. Whether they come in the midst of apparent

health or after repeated warning or under circumstances that mask their identity, they obtrude themselves precipitously. By this mark alone their significance may often be suspected and the possibility of coronary occlusion should always be considered when symptoms of myocardial disease develop suddenly, more especially when the symptoms are ushered in by pain. With this possibility in mind, a carefully taken history may point to coronary occlusion as the cause of myocardial insufficiency even after symptoms have been present for months. In the following instance the story told by the patient at once suggested this explanation and the subsequent progress of events confirmed the impression.

W. B. H., 59, male, white, married, salesman—December 1, 1919.

Complaint: Shortness of breath and high blood pressure.

Present illness: The patient's illness began very suddenly two years ago. He was on a sleeper and as he got into his berth he was suddenly seized with such severe and excruciating pain over the left side of the chest that he thought he would surely die. At the first stop he was carried from the train to a hotel and remained there for seven weeks. During the whole of this time the pain persisted, but intermittently. An hour or two would pass without pain and then it would return for a period with great severity. Even when free from it he was miserable, anxiously and fearfully awaiting its return. His blood pressure at this time was very high, in the neighborhood of 220 mm. Hg. He recovered slowly from this long illness. When he got out of bed he was very weak, and as he began to go about, he became quite short of breath. The shortness of breath has persisted since then and the least effort has made him pant. However, by exercising great care he was able to carry on his occupation of salesman in a limited way. In December 1918 he foolishly overexerted himself on a hunting trip. Dyspnea became greatly aggravated and he was forced to spend seven weeks in bed. As long as he lay quietly he was comfortable, but as soon as he got up, shortness of breath returned. In June 1918 he had a severe nose bleed lasting off and on for four or five days before it was finally stopped. He was weak and prostrated from the loss of blood. In July a severe attack of lumbago and sciatica came on and the pain forced him to spend about four months at home resting quietly. However, this enforced period of rest helped his heart little or not at all, for when he attempted to return to work six weeks ago, he soon became so short of breath that he was obliged to give up. During the past month he has grown progressively more and more dyspneic.

Past history: The patient has always been very strong and healthy. Infections: The only important illness was typhoid fever at twenty-one years of age. At forty he had a period of unconsciousness, covering about four or five days, which he attributes to a sun-stroke. No operations or accidents. Head: The patient has

occasional headaches which he attributes to over-eating. Eyes: He wears glasses for reading. Otherwise normal. Ears: Negative. Nose and Throat: He says that in childhood his throat was very delicate. Since he has grown up he has had practically no nose or throat symptoms, except on one occasion an attack of tonsillitis. Teeth: Recently eight were taken out. He has pyorrhea. The teeth have not been x-rayed. Cardio-respiratory: Negative up to the present illness. Gastro-intestinal: Appetite is good. Digestion is good. Bowels are regular. Genito-urinary: Recently polyuria. Nycturia three times. A genital sore at eighteen. Treated at Hot Springs. Neuro-muscular: The patient has always been of a very stable disposition. He says that until the attack of lumbago he never had any nervous symptoms. Weight: Usually 250 lbs. Habits: For the past twenty years the patient has been a salesman. Before that time he had no regular occupation. He took a great deal of interest in gunning and all out of door life. Alcohol—very little. Tobacco—from twenty to forty cigarettes a day and several cigars. Marital: The patient married at thirty. Wife is living. About a year ago she had a nervous break-down and is now in a hospital. The patient attributes his symptoms to worry over her condition. Four children are living and well.

Family history: Father died at the age of sixty-five from cirrhosis of the liver. Mother died at the age of seventy from cancer of the breast. Two sisters are living and well. One brother died of diphtheria at the age of three. One brother died at nineteen from typhoid. One sister died at three from pneumonia.

Examination: Weight: 239 pounds. Height: 6 foot $1\frac{3}{4}$ inches (heels about 1 inch). General Appearance: The patient is a large, well built man, considerably over weight for his height. The face is a little suffused, and the lips are a little dark in color. There are a number of dilated venules over the cheeks. Eyes: Normally prominent. Pupils equal, regular. They are much contracted. They react to light. Teeth: In very poor condition. There is marked recession of the gums and a little pyorrhea. Some of the molars have been extracted. There is extensive bridge-work over the upper central group of teeth. The tongue is clean. Throat: Somewhat injected. Tonsils small and show no evidence of infection. Lymph nodes: Negative. Thyroid: The gland is symmetrical. There is possibly one small nodule in the left lobe. Chest: Front: Is broad and thick. Costal angle about 120°. Movements about equal on the two sides. Back—the spine is straight. There are no unusual prominences of any of the spinous processes. No tenderness along the spine. Shoulders are about on a level. Movements about equal on the two sides. Lungs: The percussion note is everywhere resonant, perhaps a little hyperresonant in quality. Breath sounds are normally vesicular. There are just a few coarse, moist râles equally distributed. Back: The percussion note is everywhere resonant. Breath sounds are vesicular. There are numerous moist râles over the left lower lobe. Heart: The apex beat cannot be definitely located. There is indefinite pulsation in the fifth interspace well outside the nipple line. Cardiac dulness at the level of the fourth interspace measures 4.5 cm. to the right and 17 cm. to the left of the median line. There is no definite

impairment over the manubrium. At the apex the heart sounds are rather distant. The first sound is accompanied by a soft systolic murmur. The heart sounds all over the body of the heart are rather distant. In the aortic area there is a harsh systolic murmur. The second aortic sound is accentuated and ringing in quality. There is no diastolic murmur. The heart's action is not quite regular. Some of the beats come a little early but are not followed by a compensatory pause. They are probably auricular extrasystoles. Blood pressure: 180/70. Pulse: The pulse shows the same irregularity as the heart. The beats occasionally seem to be coupled. Occasionally a beat is dropped, at other times there is a definite premature beat. The rate is 80 to the minute. The radials are tortuous and considerably thickened. Abdomen: very prominent. There is a thick panniculus. The abdominal wall is soft and relaxed. There is a little resistance below the right costal margin, but no definite edge can be felt. Liver dulness extends two fingers' breadths below the costal margin. The spleen is not felt. Reflexes: The periosteal radials, biceps and triceps are normally active. The patellar reflexes are not definitely obtained. There is no swelling of the ankles.

Impression: The history of an acute onset of the symptoms two years ago, with severe precordial pain followed by persisting dyspnea, suggests very strongly the occurrence of a coronary thrombosis at that time. The history since is one of gradually increasing dyspnea aggravated by over-exertion. The patient entered the Johns Hopkins Hospital (History No. 42943) on December 1st, 1919, and died December 27th, 1919. Rest and digitalis somewhat relieved the dyspnea and at first he seemed to improve. The electrocardiographic report on December the 4th is as follows: Rate 66. Rhythm regular. P-R interval measures 0.16 second. The Q-R-S interval measures 0.09 second. Initial ventricular complexes are heavy in outline and conspicuously notched in leads 2 and 3. P_2 is diphasic. T_1 is inverted. Left ventricular preponderance. The type of curve suggests a terminal arborization block. On December the 6th he had a severe attack of substernal pain, which persisted interruptedly for two days and was only partially controlled by morphia. The temperature, which had been normal, rose on the 7th to 101.8°, on the 8th to 101° and then gradually fell again to normal with a slight afternoon rise. On December the 24th there was a sudden access of dyspnea and a return of the substernal pain. Later there was nausea and vomiting and cough with pinkish sputum. The temperature rose to 101° On the 25th he was still miserable with pain and dyspnea. Cheyne-Stokes breathing had come on and cyanosis was well marked. The temperature rose to 102.5°. The leucocytes which were 6,000 on admission rose to 14,000. On the 26th he was somewhat more comfortable. During the day short periods of remarkable cardiac irregularity came on. It was difficult to say whether the irregularity was due to numerous premature beats or to fibrillation. There were also short runs of rapid regular contractions, possibly brief paroxysms of tachycardia. No pericardial friction could be heard. On the afternoon of December the 27th the patient had another attack of pain followed by severe dyspnea and profuse sweating. The pulse rose from 72 to 180.

Morphia gave relief but a little later the pain returned and he vomited. At seven in the evening he died suddenly.

A. Pain. The pain of coronary occlusion is similar to the pain of angina pectoris but more severe and more prolonged. The patient may be held in the grip of almost unendurable agony for hours or even days and morphia may be powerless to relieve his suffering and may do little to assuage his pain. Older authors have graphically described the condition under the term *status anginosus*. The location of the pain and its distribution is in a general way the same as in angina pectoris. Head and Mackenzie have studied this feature in great detail and the matter is too familiar to need further comment. The one particular in which the seat of pain in coronary occlusion differs from its location in angina is a tendency to be more circumscribed and in unusual situations. For instance, one patient whom I saw complained only of excruciating pain in the left interscapular area, and if pain was present elsewhere, his memory must have been overpowered by this lancinating torture, for when it had subsided, he could recall no other. However, what I wish particularly to point out is the great frequency with which the pain is referred to the epigastrium. Hardly an author who has written about coronary occlusion has failed to comment upon this fact, and Obratzow and Strachescow were so impressed by it that they describe the *status gastralgicus* as one of the three cardinal symptoms. Often in addition to the epigastric pain there is tenderness and rigidity of the abdominal muscles, distention, nausea and vomiting. This group of symptoms, so strikingly imitative of the symptoms of a severe upper abdominal accident, has often misled physicians seriously to consider operation and at times even to undertake it.

B. Shock. The onset of pain is accompanied by all the symptoms of profound shock. The skin is blanched and has an ashen gray hue peculiar to this condition; sweat stands upon the brow; the pulse is feeble, sometimes impalpable; the patient has the terrifying aspect of mortal anguish. There is no dramatic gesture, no fuss and flurry of nerves, the imposing stillness intensifying the impression of the imminence of death. When the pain has subsided, extreme prostration continues. The patient is exhausted and only urgent dyspnea forces the activity of violent breathing. This extreme picture is not always

developed. The degree of shock is usually the measure of the severity of the accident, and if only a small vessel be plugged or the heart muscle be protected by the previous development of a collateral circulation, the symptoms of collapse may be tempered. Occasionally there is no real pain but only a feeling of numbness or oppression associated with more or less striking symptoms of shock. At times, instead of immobility, there is restless activity. In addition to pain and prostration there is usually *angor animi*. The pain may be so severe that concern about death is abolished; indeed the prospect of its speedy arrival may be welcomed. However, the grave import of the sudden access of symptoms is nearly always fully and keenly appreciated.

With the onset of the attack, and in severe instances for days after, there is a conspicuous fall in blood pressure. To recognize this constant and important symptom it is necessary to know the pressure level before the onset of the accident. A systolic pressure of 130 mm. Hg may mean nothing as an isolated observation, but it acquires far-reaching significance if previously it has regularly averaged over 200 mm. Hg. Such observations have been frequently made. At times the pressure is well below 100 mm. Hg. At other times it is too low to be accurately determined. At still other times the pulse completely fails and no radial movement can be detected. This fall in pressure is one of the important symptoms of coronary occlusion. In angina pectoris there is always a rise in pressure with the paroxysm, although the rise may be of short duration. Exceptions to this rule are very rare.

At times the blood pressure falls so low that the urinary secretion is impaired and may for a time even be suppressed. This interesting symptom has not previously been noted, but since seeing a patient who had suppression of urine for nearly forty-eight hours, I have observed three other instances of coronary occlusion with a scanty urinary output during the twenty-four hours following the accident. Experiments upon dogs and cats demonstrate that the systolic pressure must fall below 40 mm. Hg before urinary secretion stops.[3] In occlusion of the coronary artery myocardial insufficiency often de-

[3] Cushny.

velops with great rapidity as evidenced by the immediate onset of extreme shortness of breath and pulmonary edema. Under such circumstances venous stasis will augment the effect of the low pressure in retarding urinary secretion. The following report illustrates the occurrence of urinary suppression.

W. B. L., 67, male. Seen in consultation with Dr. W. W. Jarrell, April 27, 1923. On April the 4th, at about seven o'clock in the evening, while sitting quietly in his library after dinner, the patient was seized with a violent pain in the left interscapular area. The pain was intense and persisted throughout the night in spite of a number of injections of morphia totalling one grain. The patient was blanched, sweated profusely and was deeply shocked. The pulse was weak. Following the attack of pain no urine was voided for 24 hours. The nurse's chart showed an output of urine from noon April the 5th to noon April the 6th of 60 cc., during the following 24 hours of 150 cc., during the next 24 hours of 600 cc., during the next 24 hours of 1800 cc. The urine first voided was highly albuminous and contained many casts. After the fourth day there was no albumin and only an occasional hyalin cast. With rest in bed and the administration of digitalis the patient began to improve, but about one week later he had a second access of pain more easily controlled by morphia than the first but followed by extreme weakness and prostration. The blood pressure was, systolic 100, diastolic 60 mm. Hg. The patient remained prostrated, pale and somewhat cyanosed. He had persisting Cheyne-Stokes breathing with alarmingly prolonged periods of apnea. There was some cough with a small amount of serous sputum. The only important point in the past history was that during the preceding five or six years the patient had had attacks of substernal pain on exertion which often stopped him short during exercise. These attacks were associated with gas and belching and were assumed to be due to indigestion.

Examination: April 27th, 1923. The patient is lying quietly propped up in bed. He is very pale and has a striking grayish color. The immobility, the muscular relaxation, the subdued interest in what goes on about him denote weakness and prostration. There is an extreme Cheyne-Stokes type of breathing with unusually prolonged periods of apnea. The patient is conscious, but his attention is held only intermittently on account of a tendency to doze off during the long periods of apnea. He complains bitterly of the breathing, saying that he forgets to breathe and is then troubled by the necessity to breathe extraordinarily deeply. His appearance creates at a glance the impression of grave illness. The pulse is between 80 and 90, perfectly regular. The peripheral vessels show no unusual sclerosis. The blood pressure is, systolic 120 mm. Hg, diastolic 80 mm. Hg. The patient is a sparely nourished man but the apex beat of the heart is only indefinitely located. To percussion the heart is not enlarged. The sounds are quite clear but remarkably distant and feeble. The lungs are resonant, the breath sounds vesicular, but over both lungs from top to bottom are heard numerous fine moist râles

of edema. The abdomen shows nothing remarkable; the liver and spleen are not enlarged. There is a little pitting over the shins. No enlargement of any of the superficial lymph nodes. The deep reflexes are normally active. A renal function test performed by Dr. Jarrell early in May gave these results:

TIME	QUANTITY	GRAVITY	ALBUMIN	SUGAR	REACTION
	cc.				
6:00 a.m.	95	10175	None	None	Acid
8:00 a.m.	123	10167	None	None	Acid
10:00 a.m.	80	10165	None	None	Acid
12:00 m.	82	10165	None	None	Acid
2:00 p.m.	130	10166	None	None	Acid
4:00 p.m.	85	10167	None	None	Acid
6:00 p.m.	150	10167	None	None	Acid
8:00 p.m.	100	10167	None	None	Acid
10:00 p.m.	125	10157	None	None	Acid
11:00 p.m.	85	10167	None	None	Acid
2:00 a.m.	130	10170	None	None	Acid
4:00 a.m.	100	10165	None	None	Acid
Total.....	1285	10157 10175			
Average.....		10166			

The patient made a slow but satisfactory recovery. Under date of June 10, 1923 Dr. Jarrell writes: "For a while Mr. A. seemed to be improving but during the past two weeks he has slipped back and his condition at present is by no means reassuring. He has Cheyne-Stokes respiration at times, especially at night. His pulse is irregular on the least effort. Raising the arm several times in quick succession makes it miss considerably. At times with the disturbed respiration he loses consciousness momentarily and awakens with a gasp, hungry for breath. He is not voiding as much water as he drinks and is beginning to show some retention of fluid in the tissues. He has had several twinges of pain between his shoulders during the past ten days but they have not been very severe. His pulse is excitable, varying from 68 to 90 in a few minutes without appreciable cause." Again under date of August 9, 1923: "His progress has been that of a slowly rising tide. More often than not I did not have a very definite idea of his real condition, but now I am confident that he is definitely, and I may say decidedly, better." On September the 19th, 1923, I saw the patient again. He had improved rapidly during the preceding month and at this time felt remarkably well. His only complaint was shortness of breath on exertion. He was in excellent condition. The heart was not enlarged to percussion. The sounds were plainly heard and clear except that the first sound at the apex was accompanied by a soft but prolonged systolic murmur. The pulse was regular, 76 to the minute. The blood pressure,

systolic 132 mm. Hg, diastolic 80 mm. Hg. The lungs and abodmen showed no abnormality. Dr. E. W. Bridgman reports upon the electrocardiogram as follows: September 19, 1923—Pulse rate is 96 and regular except for very occasional premature left ventricular systoles. Patient's resistance is 2000 ohms. P waves are upright and monophasic in the 3 leads and show unusually low curves. The P-R interval is 0.20 of a second. R waves are of very low potential. They are diphasic in the 1st, 2nd and 3rd leads, definitely split and definitely atypical in form. Q-R-S intervals are definitely prolonged, measuring 0.12 of a second, instead of the upper limit of normal, which is 0.10 of a second. T waves are not made out in the 3 leads. Very occasionally appeared a left ventricular precocious systole, associated with full compensatory pause. The patient was not exercised.

Impression: The tracing is of unusually low potential throughout and shows upper limit of the normal P-R conduction time and definite increase in intraventricular conduction and an occasional left ventricular precocious systole.

2. SYMPTOMS ASSOCIATED WITH THE MYOCARDIAL DAMAGE; MYOCARDIAL INSUFFICIENCY

A. Dyspnea. Pain, shock and dyspnea are the three characteristic symptoms that mark the onset of coronary occlusion. At times pain is not remarkable, indeed it may be absent, and then usually dyspnea is the prominent symptom. This occurs most frequently when the accident happens to a patient already suffering from myocardial insufficiency, but it also occurs occasionally when there has previously been no evidence of impaired heart action. There is nothing peculiar about the dyspnea except the sudden onset and in severe instances the intensity. Wearn speaks of a patient seated quietly in the house at the time of onset when he was suddenly seized with such urgent dyspnea that he ran out of doors to get air. However, just as pain may vary from the most intense agony to mild sensations of constriction or oppression, so may dyspnea at times be slight and transient. It is seldom, if ever, altogether absent.

B. Passive congestion. In the train of dyspnea follow the characteristic symptoms of passive congestion. Chief among these are cyanosis and pulmonary edema. Cyanosis comes on early, is often extreme, and persists through convalescence. The peculiar pale, ashen hue, so characteristic a part of the facies of the disease, is caused by the admixture of cyanosis with the pallor of shock. Sometimes, and more particularly days or weeks after the occlusion has occurred,

cyanosis persists even after dyspnea has disappeared. The striking appearance of the patient may then at once suggest the possibility of coronary occlusion and in the light of this suggestion a careful review of the history and the other symptoms may lead to a correct diagnosis.

Pulmonary edema is such a constant accompaniment of coronary occlusion that it is an important part of the clinical picture. With severe or even moderately severe symptoms it is never absent. Moist râles may be present only over the lower lobes, or fine crisp râles may be heard over both lungs from apex to base. At the same time there is often acute distention of the lungs and the distention and edema may be important factors in augmenting the dyspnea. There is usually an irritative, hacking cough which may occasionally be persistent and exhausting. The cough may produce small amounts of serous sputa frequently streaked with blood and frankly bloody if pulmonary infarction has occurred. Occasionally, pleural effusion develops either as a symptom of stasis or in association with pulmonary infarction.

There is nothing remarkable about the other symptoms of passive congestion which usually come on gradually, if they appear at all. The liver often swells, albumin may appear in the urine and edema in the subcutaneous tissue. Libman has suggested that early and marked swelling of the liver points to occlusion in the right rather than in the left coronary artery.

C. Cheyne-Stokes breathing occurs so commonly after coronary occlusion that it deserves mention as a detail of the clinical picture.

D. Upon examining the heart the conspicuous, the impressive feature that at once attracts attention is the remarkable contrast between the symptoms of myocardial insufficiency that have been observed and the entire lack of local manifestations of cardiac disease. For as a rule when the heart fails it is already hypertrophied from years of increased labor, and diffuse pulsations proclaim violent though ineffectual beating. In coronary occlusion we turn from beholding dyspnea, cyanosis, collapse to look upon the chest and are startled to see there no sign of tumult nor of effort. Indeed, the throbbing usually present in health may be absent. We search for the apex

beat with eye and finger and do not find it. We listen and the heart sounds come to the ear faintly as though from a great distance. Even the area of cardiac dulness may not be enlarged. These unaccustomed circumstances may mislead one to detach attention from the heart, and if epigastric pain, distention and nausea be present, to fasten it upon the abdomen. However, reflection will at once make it clear that these signs are the characteristic symptoms of feeble heart action and just the symptoms one would anticipate finding if coronary occlusion occurred in a heart not previously altered by disease. If the heart is already hypertrophied as a result of hypertension or valvular disease, feeble impulse and distant sounds are not conspicuous. However, a diminution in the force of the impulse and in the intensity of the sounds might be noted in patients who had been repeatedly observed prior to the accident.

Cardiac infarction may leave existing murmurs unaffected; or, a systolic murmur previously noted may disappear with the enfeeblement of the beat; or, again, a systolic murmur may make its first appearance. There is nothing of importance in these manifestations nor of help in diagnosis. Gallop rhythm often comes on to betray embarrassed heart action and at times the sounds take on the quality and rhythm designated embryocardia or tic-tac rhythm.

Irregularities of cardiac rhythm are very common. Only a small proportion of the cases show constantly a regular pulse. Premature beats are the commonest type of irregularity, the ventricular form being much more common than the auricular. Auricular fibrillation, auricular flutter, heart block, pulsus alternans and paroxysms of tachycardia frequently occur. Ventricular tachycardia, otherwise rare, is not uncommon in cardiac infarction, and its appearance is ominous, since it is often followed by ventricular fibrillation. One or more of these various types of irregularity may follow one another or occur together. I should emphasize further a tendency to marked variation in rate, especially upon exertion. I have seen the pulse suddenly rise from eighty to a hundred or more as the patient sat up in bed. These patients were not studied electrocardiographically so I cannot say with certainty that an abnormal mechanism was absent. Still the pulse was perfectly regular and the change in rate seemed to arise at the sinus.

3. THE SYMPTOMS ASSOCIATED WITH THE MYOCARDIAL INFARCT

A. *Fever* and *leucocytosis* are seldom absent. The temperature may rise a few hours after occlusion occurs, but usually begins after twenty-four hours. It rises to between 100° and 101° but may go to 102° and higher. In some instances it subsides after three or four days but it may persist for weeks. The leucocytes are usually from 12,000 to 15,000 and seldom exceed 20,000 per cmm. The fever and leucocytosis must be caused by absorption of necrotic material from the infarcted area. It is hardly necessary to point out their importance for diagnosis. They are a valuable aid to distinguish coronary occlusion from angina pectoris and myocardial insufficiency due to other cause and unless one is familiar with the occurrence of fever and leucocytosis with cardiac infarction, their presence may be held to favor an abdominal accident in the presence of symptoms simulating abdominal disease.

B. The *pericardial friction* that is sometimes heard over a cardiac infarct has been sufficiently stressed as an important aid to diagnosis. When present, it deserves all the emphasis that has been put upon it. To hear a pericardial friction under circumstances that suggest the occurrence of coronary occlusion is practically to establish the diagnosis. However, there is a great difference of opinion about the frequency with which a rub can be detected. Gorham heard it in five out of six instances of coronary occlusion that he observed. Gordinier in eleven of thirteen consecutive instances examined by him. On the other hand, a pericardial friction was discovered in only two of the nineteen cases reported by Wearn and in none of Longcope's sixteen cases. I myself have heard it but once in a series of ten cases, although most of these patients were seen days or weeks after the accident had occurred and then at but a single visit. Gorham has reviewed the question in detail and a full historical note may be found in his article. He points out that the rub is of light intensity, transitory in nature, often recurrent and localized over a small area. It may be heard at one visit, missed at the next and heard again the following day. Unless listened for repeatedly and with great care, it may easily escape detection. Both experimental and pathological evidence demonstrates that most cardiac infarcts have their base upon the inner

surface of the heart rather than upon the outer[4] and only a small number of the hearts studied after death have shown pericardial exudate. However, it is true that the exudate may be slight and may soon be absorbed, and its absence at autopsy is no proof that a pericardial rub may not have been heard during life. All one can say is that when a friction is detected, it is one of the most valuable bits of confirmatory evidence we can obtain; on the other hand, when it is absent, the diagnosis of coronary occlusion is in no sense thereby contradicted.

C. Embolic phenomena, in my experience, occur more commonly than a pericardial friction and their significance is equally decisive for diagnosis. It has already been pointed out that cardiac infarcts usually, but not always, involve both chambers of the heart. This is particularly true of infarcts that follow occlusion of the ramus anterior descendens which is the branch most commonly obstructed. When the infarct, as it generally does, reaches to the inner surface of the heart, thrombi form upon the roughened surface and bits are often broken loose and float free in the chamber. Those from the right ventricle go to the lungs and produce the characteristic symptoms of pulmonary infarction; those from the left ventricle enter the general circulation and the symptoms that follow depend upon the location where they lodge. Frequently, they are swept to the brain, to the cord, to the liver, to the kidneys or obstruct large vessels in the extremities. It seems to me that these embolic phenomena, so significant for diagnosis, have not received the attention they deserve. Wearn does not mention them, nor does Longcope. One of Gordinier's patients had pulmonary embolism and he speaks of its diagnostic aid. Paullen's patient suffered an embolism to the femoral artery. Thayer has a number of pertinent instances. I should emphasize particularly the importance of pulmonary embolism in the diagnosis of cardiac infarction and two instances at once come to my mind. In one of these pulmonary embolism confirmed the diagnosis already made, but nearly proved to be fatal; in the other, of particular interest from the standpoint of diagnosis, the presence of pulmonary

[4] This fact is commented upon by Acker, Oppenheimer and Rothschild and by Smith.

infarction led by proper reasoning to the correct diagnosis of coronary occlusion. A brief account of this case is added.

J. E. C., 69, male, white, married, farmer. Admitted to the Johns Hopkins Hospital August 22, 1922—died August 31, 1922. Medical history number—48,000.

Complaint: Indigestion.

Present illness: Last April one morning after breakfast was taken with an acute pain in the lower chest and epigastrium. The pain was not sharp but racking in character. He had trouble with breathing at the same time. He says there had been absolutely no shortness of breath before that time, not even on the day before. He did not go to bed that first day but sat around after seeing the doctor for the pain. He thinks he could have worked if it had not been a rainy day. A cough started at this time. He was up and around for a week when he had another spell at the same time of day, worse than the first. He had the doctor and went to bed. He says the doctor gave him nitroglycerine which nauseated him but did not relieve the pain. During the worst spells the pains radiated down the arms. No worse on the left than on the right. He was in bed three or four days. Since then has not been able to work. He has had trouble getting up the stairs on account of shortness of breath and weakness. Has not been in bed constantly until three days ago. He went to bed at that time and finally came up to the hospital to get better care. Since the first two attacks of pain he has had occasional slight attacks of indigestion with pain. He has had a bad cough since the first attack in April. No sputum was brought up all summer but three days ago he began to raise pure blood. Never any hemoptysis before. A little swelling of the ankles during the past two weeks. Appetite has been steadily decreasing until recently he has taken only a little milk. No vomiting and no pain except during the attacks already described. He has lost a good deal of weight since April but does not know how much.

Past history: The patient was well as a child and young man. Infections: Measles, mumps, whooping cough, chickenpox, influenza. No typhoid fever, diphtheria, scarlet fever or rheumatic fever. Head—subject to headaches all of his life. No dizziness. Eyes—uses glasses for reading. Says he has seen double at times. Ears: Negative. Nose and throat: Negative except for a little catarrh in the nose. Does not catch cold easily. No tonsillitis and no quinsy. Mouth: Has had a good deal of tooth-ache. Nearly all of his teeth have been extracted. The tip of the tongue has been sore off and on for the past five years. Cardio-respiratory: Negative. No cough. No hemoptysis. No shortness of breath. No night sweats. No oedema. Gastro-intestinal: Appetite never very good. Off and on has had sharp pain in the abdomen after eating. Bowels regular. Genito-urinary: No urinary difficulties. Nycturia once occasionally. No venereal infection. Marital: Married twenty-seven years. Wife is living but is in an asylum. Seven children living and well. No miscarriages. Operations and

Accidents: None. Neuro-muscular: Five years ago he had a fainting spell which came on just after breakfast and lasted for ten or fifteen minutes. Thinks it was due to indigestion.

Examination: General appearance—the patient is a poorly nourished man who has obviously lost a great deal of weight. The skin and the mucous membranes are very pale, suggesting a marked anemia. Propped up in bed but no dyspnea. Coughing constantly and bringing up large amounts of dark brown blood. Eyes: show nothing remarkable. Eye Grounds: the discs are clear. The retinal arteries are a little tortuous and slightly thickened. The retinae are not so pale as might be anticipated from the color of the skin. Teeth: only a few teeth remain. These are in very bad condition. The tongue shows a little atrophy along the border but no marked papillary atrophy as is seen in pernicious anemia. Throat: shows nothing remarkable except the pallor. Lymph nodes: No glandular enlargement. Lungs: Show dulness over the right lower front and back where the breath sounds are diminished in intensity and many moist râles are heard. A small number of moist râles at the left base. Heart: Just a little enlarged to the left. The sounds are clear but very faint. There is marked cyanosis and striking engorgement of the jugular veins. The peripheral vessels are tortuous and extremely sclerosed. Liver somewhat firm; surface smooth. Spleen not definitely felt.

Impression: The outstanding features are the large pulmonary infarction and the myocardial insufficiency. There is no evidence of venous thrombosis as a possible source of pulmonary emboli. It is noteworthy that the heart is relatively but little enlarged, for mural thrombi seldom occur when the heart is not markedly dilated. The sudden onset with pain and shortness of breath, the increasing myocardial insufficiency and the pulmonary infarction all point clearly to coronary occlusion as the cause of the symptoms. Blood examination: Hbg, 75 per cent, R.B.C. 5,616,000, W.B.C. 26,000. A rough differential showed 95 per cent P.M.N. The Wassermann test was negative. The urine showed a trace of albumin and a small number of hyalin and granular casts. The specific gravity ranged from 1020 to 1030. The phthalein output for two hours was 37 per cent. The stool showed nothing abnormal. Blood chemistry: non-protein nitrogen 73.2 mgm. per 100 cc. Blood sugar 0.116 per cent. Blood chlorides 461 mgm. per 100 cc. Blood culture negative. Electro-cardiographic report: Rate 86. Rhythm regular. The P-R. interval measures 0.17 of a second. T waves are about flat. Voltage is low throughout.

Course after admission to hospital: During the first few days there was no noteworthy change in the patient's condition. On the 26th he had what is described as a sinking spell, characterized chiefly by weakness and great dyspnea. There was marked Cheyne-Stokes breathing with long periods of apnoea. From that time on he grew progressively weaker, more and more short of breath and became delirious. On the afternoon of the 31st dyspnea was particularly marked. On that day the percussion note over the right base was flat. The breath sounds in

this area absent. The patient gradually grew weaker and weaker and died of myocardial insufficiency at 11.15 p.m.

Autopsy number—7119.

Anatomical diagnosis. Arteriosclerosis; coronary sclerosis; thrombosis (old) in anterior descending branch of the left coronary; healed infarction of left ventricle and tip of right; mural thrombi, left and right ventricle; embolus and thrombosis of pulmonary arteries; infarction, lower and middle lobe right lung; small infarct of upper right lobe; infarct lower lobe left lung; pleural effusion, right; bilateral fibrinous pleurisy; slight chronic diffuse nephritis; cholelithiasis; chronic passive congestion liver and lung; phlebolithiasis in spleen and liver; fat necrosis about and in pancreas.

D. The necrotic infarct softens, is gradually digested and absorbed and is finally replaced by scar tissue. This scar often yields and bulges, forming an aneurysmal sac. Since the infarct is usually located at the apex this is the favorite seat of cardiac aneurysms. A consideration of this condition comes more properly under the late manifestations of coronary occlusion and it is only mentioned here because exceptionally a softened infarct will rupture and cause sudden death soon after the occurrence of occlusion.[5]

4. ADDITIONAL SYMPTOMS

Certain *associated symptoms* deserve separate mention on account of their importance in diagnosis. Chief amongst these are the gastro-intestinal symptoms.

A. It has already been remarked how frequently the pain of coronary occlusion is epigastric in location, and since the chief diagnostic error is to consider the symptoms of coronary occlusion to be due to abdominal disease, this peculiarity may properly be noted again and again. There is an intimate relation between abdominal symptoms and cardiac disorders. Patients with angina pectoris mostly ascribe their symptoms to indigestion and tell in detail how abdominal distention precipitates the pain which quickly disappears as gas is eructated. They beseech the physician to rid them of gas or to prescribe some remedy to dislocate and expel it, confident that in this way their attacks will be prevented or at least frustrated. In coronary occlusion also, flatulence, distention, nausea and vomiting appear

[5] Consult: Brunn; Kennard; Hopkins; Reznikoff; Lemierre et Piedelièvre.

frequently, and occasionally there is diarrhea and jaundice. The abdomen at times is tender and there may be marked muscular ridigity. No wonder then that experienced physicians, as we shall later illustrate, are sometimes led astray and diagnose gall-stone colic, rupture of a gastric ulcer, general peritonitis and so on, and occasionally even advise operation.

B. I have spoken casually of the *facies* of coronary occlusion and now comment upon them more minutely because they too have an important place in diagnosis. At the onset of the attack the patient is blanched, anxious, deeply shocked; the features are pinched and the expression portrays intense suffering and mental anguish; the skin is cold and covered with sweat. As the pain diminishes there is extreme weakness, prostration, dyspnea and cyanosis. The skin soon takes on a peculiar ashen gray hue. Libman thinks the description of Sansom fits it best. "It is a leaden tint spread over an earthy hue of skin." There is something extraordinary about this peculiar color and it is so characteristic that its presence immediately suggests coronary occlusion. It may persist for months after the accident has occurred. However, it is not always present and its absence is unimportant.

C. Vasomotor phenomena are often present. Blanching and sweating, the most commonly observed, have been mentioned. Sweating is sometimes profuse, sweat actually pouring from the body. Wearn mentions the occurrence of transient flushing associated with a sensation of intense heat.

D. Patients as a rule remain conscious, although when there is extreme myocardial insufficiency they may rapidly become unconscious and remain so until they die. There is usually a clear appreciation, not of the nature but of the gravity of the accident—*angor animi*. Fainting may occur after slight exertion and occasionally the patient has convulsions. Convulsions may be associated with heart block.

A separate description of the detached symptoms of coronary occlusion gives no clear impression of the varied manner in which they combine to produce the clinical picture of the disease. Having become familiar with the character and the mode of origin of the isolated symptoms a clear impression of the clinical picture can be gained only

by observing their development in patients or by noting their occurrence in the reports of cases that abound in medical literature. Even a slight acquaintance with the symptoms will prepare a physician to recognize at once severe and typical instances of the disease. However, it is desirable that he should also recognize the mild and less outspoken manifestations. In order to do this he must keep the possibility of coronary occlusion in mind and under appropriate conditions search for the features that betray it. In a rough way we may divide the symptom groups into six classes:

1. Instances in which death follows immediately upon the occlusion.
2. Instances in which death follows a few minutes, a few hours or at most a few days after the occlusion.
3. Instances in which grave symptoms of myocardial insufficiency immediately follow the accident, but in which death is postponed for weeks or months.
4. Instances with grave symptoms easily recognized but from which, after a more or less stormy course, the patients recover.
5. Instances without grave manifestations but with sufficiently characteristic symptoms to be recognized.
6. Instances with but mild and uncertain symptoms in which only a suggestive or probable diagnosis can be made.

When death comes instantaneously, coronary occlusion may be surmised but cannot be definitely diagnosed. It is probably the cause of death if the patient is over fifty years of age, shows evidence of general arteriosclerosis and particularly if there is a history of previous attacks of angina pectoris. The last named point should be emphasized, because the history is often obscure and must be diligently sought out before it is clearly exposed. Such careful searching will reveal that the final closure of a coronary artery is usually preceded by symptoms of angina pectoris. The symptoms are often mild and may pass unnoticed or be misinterpreted until their true significance is revealed in the final dramatic event. I saw a patient who was stricken suddenly in the midst of apparent health with the most agonizing symptoms of coronary occlusion. He was extremely ill and for weeks hovered about the threshold of death but in the end made a good recovery. He was sixty-seven years of age and his youthful vigor and endurance were admired and envied by all his

friends. The blow came like a bolt out of the blue sky. An inquiry into his past history disclosed nothing but mild attacks of indigestion for which he had consulted a gastro-intestinal specialist some years before. However, these attacks of epigastric pressure and gas that often stopped him short in the midst of exercise, and then with belching vanished as quickly as they came, now acquired a new and sinister meaning. The death from coronary occlusion is often extraordinarily sudden. Even pulmonary embolism is seldom so abruptly fatal, for there is usually at least a cry, a gesture or a gasp. In coronary occlusion death often strikes instantaneously, in the midst of a word or a movement, and life escapes without a tremor or a sigh. The patient is congealed in the very attitude of the unfinished act. There seems here to be something more than instant stopping of the heart. We are familiar with prolonged diastolic pauses, for instance, in heart block, during which life flows on and seconds may elapse before consciousness is lost. Allbutt explains the phenomenon of instantaneous death as a vagal reflex, but in the absence of convincing evidence the explanation does not satisfy. Possibly the two events working together may be the cause. That there is a reflex action of profound and far reaching operation is demonstrated by the extreme shock and fall in blood pressure that immediately follow coronary occlusion. If the heart continues to beat the circulation may yet be sustained; if it too fails, instant death may follow. Experiments upon dogs have shown that sudden stoppage of the heart following coronary ligation is due to ventricular fibrillation. The same mechanism probably obtains in man. Lewis, in his animals, observed the occurrence of single ventricular premature beats, then ventricular tachycardia, then ventricular fibrillation. Robinson and Hermann have reported a number of instances of ventricular tachycardia in man associated with coronary occlusion or with symptoms strongly suggesting coronary occlusion. If we are justified in assuming that cardiac standstill is due to ventricular fibrillation, then we can easily understand that the immediate effect of coronary occlusion may be determined by the location rather than by the size of the infarction. With the sudden cessation of the blood flow to the area of the heart supplied by the affected vessel, there must immediately begin profound chemical changes in the muscle. These changes may be sufficient to alter all

the relations of impulse conduction and may induce the conditions that precipitate fibrillation. Therefore, we may conceive that a large infarct may be relatively innocuous, whereas a small one may be instantly fatal. The experimental evidence assembled by de Boer lends some support to this view.

Patients who live for a few hours or days after the onset of the accident usually present such striking symptoms that the diagnosis is not difficult. The sudden onset, the intense, enduring pain, the dyspnea and cyanosis, the pulmonary edema, the profound shock, are all very characteristic.

Less severe instances of coronary occlusion followed by the symptoms of myocardial insufficiency may easily be overlooked, especially if the patient be seen for the first time when these symptoms are well developed. The signs of myocardial insufficiency then dominate the picture and the symptoms that ushered it in may be ignored or but dimly remembered. It is pertinent to remark again that the sudden onset of myocardial insufficiency should always awaken suspicion. If the sudden attack was with pain or if it was followed by fever and leucocytosis or embolic phenomena, the suspicion is greatly strengthened. A pericardial friction establishes the diagnosis.

From the standpoint of diagnosis we are especially interested in the recognition of the mild cases in patients who make a prompt and satisfactory recovery. The frequency with which the late results of unsuspected coronary occlusion are found at autopsy should stimulate us to look carefully for the clinical manifestations that may betray its presence. Any symptoms of myocardial disease that come on suddenly should be suspected, especially sudden onset with pain. The accompanying symptoms already described should then be diligently watched for. If the physician is warned and observes intelligently and carefully, the correct diagnosis will more often be made.

ASSOCIATED DIAGNOSTIC CRITERIA

Age: Coronary occlusion is in most instances, over 90 per cent, associated with sclerosis of the coronary arteries. It is therefore an accident of late adult life. It is uncommon before fifty years of age and excessively rare before forty. In eighteen of Wearn's nineteen cases the patients were over forty, most of them beyond sixty. Of

Longcope's sixteen patients two were below fifty, eight were between fifty and sixty, five between sixty and seventy and one was over seventy. Gordinier reports thirteen cases; one patient was forty-eight, four between fifty and sixty, five between sixty and seventy, two over seventy; of one the age is not given.

Sex: The disease occurs more often in men than in women. In Wearn's series there were ten men and nine women but other reports show a greater male incidence. Gordinier has ten men and three women. All six of Gorham's patients were men. Faulkner, Marble and White report thirty cases, twenty-four in males and six in females. Of the last ten cases I have seen only two were in women.

Arteriosclerosis and hypertension: In most instances the patients display generalized arteriosclerosis. However, as is well known, there is no constant relation between the condition of the coronary arteries and the condition of the peripheral vessels. Still, a suspicion of coronary sclerosis receives some support when there are well marked arterial changes elsewhere. Libman advises a careful inspection of the arteries of the legs.

It is impossible to say how frequently hypertension accompanies coronary disease. That there is no close relation between the two is certain and often there is extensive coronary sclerosis when the blood pressure is normal. However, arteriosclerosis and hypertension so commonly go together that I am inclined to believe an elevated blood pressure often precedes coronary occlusion. There are no available figures from which to draw conclusions, for most reported cases were first seen after the accident had occurred and blood pressure observations made at that time are no indication of what the pressure may previously have been.

Syphilis: Syphilitic infection is an uncommon cause of coronary occlusion. This is as one would anticipate. Syphilis causes extensive disease at the root of the aorta but seldom invades the coronaries. When it causes coronary occlusion, it does so by obstructing the mouths of the coronary arteries. None of Wearn's nineteen patients gave a history of syphilis and the Wasserman test performed upon thirteen was negative in all. Syphilitic aortitis was not disclosed at autopsy. Of Longcope's seventeen patients two gave a positive Wassermann reaction. At autopsy one of these showed a typical

syphilitic aortitis with occlusion of the mouth of the right coronary artery. Of the thirty cases reported by Faulkner, Marble and White, in four syphilitic aortitis was present.

Antecedents: There is nothing in the previous history of the patient that is important except the occurrence of attacks of angina pectoris. Enough has already been said about this and about its value in diagnosis. Occupation, habits, station in life have no direct bearing upon the condition. There is a generally accepted belief that angina pectoris and coronary disease are peculiarly common to men of intellectual habits and to men who have held positions of responsibility and importance. In contrast to this it is said to be uncommon among artisans, laborers and the whole group of poor patients which crowds our dispensaries and free wards. The contrast is remarkable, because among such patients all of the other manifestations of arteriosclerotic disease abound, indeed are conspicuously prominent. The contrast is probably one of interpretation rather than of occurrence. A characteristic feature of angina pectoris is that its effects are manifested by sensations not by objective signs. These sensations are keenly appreciated by the intellectually alert and fluently transmitted into words, whereas in the intellectually obtuse they are dully perceived and remain inarticulate. Therefore, angina pectoris will always be a disease of the refined, intellectual classes, but the dramatic manifestations of coronary occlusion will occur equally often in all.

ELECTROCARDIOGRAPHIC STUDIES[6]

Until now I have said nothing about the evidence of coronary occlusion disclosed by the electrocardiogram. This apparent neglect is not meant to slight the evidence, for it is very important, but the consideration of it was postponed so that it might be weighed and judged in some detail. The value of the electrocardiogram in faithfully portraying alterations, be they ever so slight or intricate, of rhythm, is now fully accorded. In coronary occlusion this value is especially serviceable, since changes in rhythm are frequent, often transient and sometimes complicated. Without its aid it is often

[6] For details consult: Smith, Pardee, Willius, Brown, Bousfield, Oppenheimer and Rothschild.

difficult to distinguish auricular from ventricular premature beats; auricular flutter may be completely overlooked and transitions from flutter to fibrillation may be missed; slight grades of heart block are difficult to recognize and delayed auriculo-ventricular conduction without dropped beats cannot be appreciated; ventricular tachycardia cannot be recognized. All of these abnormalities and any combination of them are clearly shown by the electrocardiogram. I have already referred to the significance of ventricular tachycardia, for it seldom occurs except in connection with cardiac infarction. The remaining arrhythmias are in no way peculiar to coronary occlusion, but their sudden onset in conjunction with other suggestive symptoms is important corroborative evidence, especially if they are transient or vary quickly from one type to another.

Of greater interest than the arrhythmias in relation to the diagnosis of coronary occlusion are those electrocardiographic changes which are interpreted to indicate serious myocardial damage. About the significance of heart block there is no question; undoubtedly it indicates damage of some kind to the auriculo-ventricular bundle of His. Bundle branch block, which nearly always affects the right branch, is equally definite in its implication. However, there is still some uncertanty about the interpretation of those electrocardiographic changes which are held to denote alterations in the finer ramifications of the neuro-muscular conducting system, changes that are spoken of as arborization block. In these electrocardiograms the ventricular complexes show, (1) prolongation of conduction time; (2) notching of the main deflection; (3) low voltage in all three leads; (4) absence of the large T waves characteristic of bundle-branch block. In addition to these abnormal ventricular complexes great emphasis has been placed upon inversion of the T wave.

Smith was the first to study in detail the electrocardiographic changes that follow ligation of different branches of the coronary arteries in dogs. Premature beats were frequently noted. Often there were short runs of three or four followed by permanent tachycardia, ventricular fibrillation and death. Ventricular fibrillation invariably followed permanent ventricular tachycardia, but was not always preceded by it. Occasionally, auricular flutter and fibril-

lation developed. He emphasizes particularly changes in the T wave not previously described. There was almost constantly a change from the strongly positive peak to a markedly negative one and then a gradual return to the positive or isoelectric form. Later Smith reports observations upon eleven patients with coronary occlusion. Eight of the eleven patients showed characteristic changes in the T wave. Smith also emphasizes decrease in the amplitude of the QRS group, an abnormality discovered in six of the patients. He points out that these changes come on soon after the occlusion has occurred and there is a slow return to normal. It is important, therefore, to take electrocardiographic records as soon after the coronary closure as possible and to repeat observations at frequent intervals. Curves taken after a week or two may fail to show the characteristic changes. Pardee calls attention to further abnormalities of the T wave. Records taken from a patient shortly after the onset of occlusion show the T wave arising from the descending limb of the R wave, sometimes near the isoelectric point, at other times near the tip. In a word, the T wave is continuous with the R wave and the usual isoelectric pause between the two is absent. The T wave is usually inverted in lead II and in one other lead.

These electrocardiographic changes unquestionably denote alterations in the heart muscle. The nature of these alterations must be decided upon other evidence. Sometimes there is no gross demonstrable lesion, at other times the damage is transitory, at still other times there is extensive permanent myocardial disease. The electrocardiogram cannot make a diagnosis of coronary occlusion, it can only indicate changes in the heart muscle. However, such an indication considered in conjunction with all the other clinical evidence may have an important bearing upon diagnosis. Experience alone will tell us just how important this bearing may prove to be. I need only add, what has already been intimated, that the absence of these electrocardiographic abnormalities does not exclude the diagnosis of coronary occlusion. A single examination, and particularly a single late examination, may fail to show alterations that might appear in records taken frequently and more especially shortly after the accident.

PATHOLOGICAL ANATOMY

There are four possible causes of coronary occlusion:

1. Disease of the coronary arteries
2. Thrombosis
3. Disease at the root of the aorta
4. Embolism

The chief cause of occlusion is arteriosclerosis of the coronary arteries, and the final closure is usually due to thrombosis. These two factors work together. Arteriosclerosis alone would cause complete obstruction of the vessel so slowly that time would be given for a compensating collateral circulation to develop. Under these circumstances final closure of the vessel might occasion no alarming symptoms. However, sclerotic changes are seldom carried so far. When the vessel has become markedly diseased, but long before the inner walls are approximated, thrombosis usually occurs and the blood flow is abruptly stopped. Thrombosis never happens in a healthy vessel. Disease at the root of the aorta may cause obstruction by compressing and sealing over the mouths of the coronary arteries. This seldom comes on in arteriosclerotic disease but more often in luetic aortitis. Luetic lesions rarely invade the coronaries themselves. Embolism is an unusual cause of occlusion. When it occurs, it is nearly always due to a bit of vegetation broken loose from the aortic valve or to a ribbon of vegetation waving in the blood stream and finally floating into the coronary artery.

In Wearn's nineteen cases arteriosclerosis was the essential lesion in all. In eighteen, thrombosis caused the final obstruction. In one a thrombus was not found, the vessel being practically occluded at one point by an atheromatous constriction. In sixteen instances the ramus descendens anterior was the vessel blocked. The posterior descending branch of the left coronary was thrombosed in one, the descending branch of the right coronary in one, the posterior circumflex branch of the left in one. In Longcope's seventeen cases an occlusion of one or more important branches of the coronary arteries by a sclerotic process occurred in six; occlusion by thrombi always associated with sclerosis, in ten; occlusion by embolus in an otherwise normal artery in one. One of the patients had a typical luetic aortitis

with occlusion of the mouth of the right coronary artery by this process. Of the thirty cases reported by Faulkner, Marble and White, twenty-five showed arteriosclerosis of the coronary arteries; four, syphilitic aortitis; one, vegetative endocarditis with embolism. The anterior descending branch of the left coronary artery was occluded in twenty-two; the left coronary artery at its orifice in two; the right coronary artery in five; the circumflex branch of the left coronary artery in one. Lamb reports an interesting instance in which a floating mass of vegetation completely plugged the left coronary artery. MacCallum reports a case in which death followed at once upon occlusion of the anterior branch of the left coronary artery by a loose vegetation. Occasionally, an aneurysm forms upon the coronary artery. This may rupture or finally cause occlusion of the vessel by thrombosis. Fraenkel describes an interesting instance in a young man twenty years of age, which apparently followed trauma. His and Beitzke report a remarkable condition of dilatation and thrombotic occlusion of both coronary arteries in a young man of twenty. No cause was discovered to account for the extraordinary condition. Le Count gives an interesting analysis of sixty cases of death following disorders of the coronary circulation. Of thirty-six persons dying from obstruction of the coronary arteries, the occlusion was caused by thrombosis in twenty-nine; by syphilitic disease sealing the mouths of the coronaries in four; by embolism from ulcerative endocarditis of the mitral valve in one; by acute dissection of the wall of the circumflex branch of the left coronary in one; by rupture of the coronary artery in one; occlusion by calcareous masses, which were loosened in the channels by softening of patches of atheroma, in one. The pathological anatomy of the cardiac infarct is well described by Karsner and Dweyer.

PROGNOSIS

There is not at hand enough statistical evidence from which to deduce a satisfactory prognosis of coronary occlusion. In describing the dramatic symptoms of the accident all has been said that may properly be said upon the subject. It is frequently fatal and still patients desperately ill may finally recover and live on for many useful

and contented years. It is comforting to emphasize this favorable outlook upon the situation. One patient whom I saw had an attack of coronary occlusion from which he recovered and remained well for three years. He then had a second attack with pulmonary embolism to which he nearly succumbed. However, in the end he regained his health and was well and active for four years, when suddenly the third attack came on which was fatal. Thayer reports a remarkable instance of recovery. Following coronary occlusion the patient developed grave symptoms of embolism to kidneys, spinal cord and both iliacs. Yet he recovered and was well for eight years when anginal symptoms returned and after several months, marked by recurring attacks, he died suddenly. Up to the present time the diagnosis of coronary occlusion has been made only when the accident has been accompanied by grave and characteristic symptoms, that is, when a large coronary branch has been plugged and a large area of infarction has followed. I cannot escape the conviction that milder manifestation of the accident are not altogether uncommon, and I believe that as the subject attracts wider attention the diagnosis will be more often made. This conviction draws some support from the fact that autopsy often reveals the evidence of previous myocardial infarction which had passed unrecognized during life.

DIFFERENTIAL DIAGNOSIS

Since the symptoms of angina pectoris are similar to the symptoms of coronary occlusion there may be difficulty at times in deciding whether an attack is really due to plugging of a coronary artery. The symptoms of the two are not only alike, but the actual anatomical lesion underlying both is often the same; for in spite of Albutt's erudite and brilliant argument to the contrary the conviction remains that sclerotic changes in the coronary arteries is a common cause of angina pectoris. Nor is this conviction a stubborn and unwarranted adherence to tradition and accepted opinion. The most obvious facts confirm it. Death in an attack of angina is nearly always due to coronary occlusion and coronary occlusion is nearly always preceded by recurring attacks of angina, although the attacks are often masked.

The implication of this clinical course of events is fully corroborated and enhanced by the evidence of autopsy. One would not be justified in saying that disease of the coronary arteries is always the cause of angina, but that it is one cause and an important cause is beyond doubt. A small coronary branch may be plugged and give no signs that distinguish it from an attack of angina; a large branch may be so slowly occluded that only a transitory pang, or indeed no symptoms at all, may accompany the final closure; but if a large branch is suddenly shut off and an infarct forms, the distinction from an ordinary attack of angina is clearly marked. The distinguishing marks are these: The pain is usually more severe and more prolonged; the patient who has previously suffered from attacks of angina recognizes at once that something extraordinary has happened, something different from what has gone before. Prostration is more profound and is accompanied by a conspicuous fall in blood pressure, whereas angina is almost invariably accompanied by a rise in pressure. Fever and leucocytosis then come on and usually, too, the symptoms of myocardial insufficiency. I pause to emphasize again the great value for diagnosis of fever and leucocytosis! If now a pericardial friction is heard or if embolic phenomena appear, the clinical picture is then complete.

The symptoms of myocardial insufficiency may obscure and even cover over the symptoms of coronary occlusion. If the accident happens to a patient already suffering from myocardial insufficiency, it may be difficult and even impossible to recognize. In patients presenting the cardiac symptoms of arteriosclerotic disease any sudden aggravation of the symptoms should arouse suspicion. In patients past middle life without valvular disease, the abrupt onset of myocardial insufficiency should stimulate a careful search for other symptoms of coronary occlusion.

There are certain accidents to the heart and aorta which it will always be difficult to distinguish from coronary occlusion. Rupture of the aorta immediately comes to mind. A colored man entered the Johns Hopkins Hospital after an attack of excruciating substernal pain. He was thought to have coronary occlusion until autopsy disclosed a tear in the inner wall of the aorta producing a dissecting

aneurysm. Rupture of a branch of the coronary artery[7] and rupture of the heart itself may cause similar symptoms.

I have already more than once referred to the possibility of mistaking the symptoms of coronary occlusion for the symptoms of some grave abdominal disorder. Coronary occlusion may be followed by severe abdominal pain, rigidity and distention, nausea, vomiting, diarrhea and even jaundice. Absence of the usual signs of cardiac disease may distract attention from the heart, and the symptoms of profound shock together with fever and leucocytosis may complete the picture of abdominal disease. If anyone is sceptical about the possibility of making such an error in practice, I ask him to read the instructive instances reported by Levine and Tranter. Acute pancreatitis, rupture of a gastric or duodenal ulcer, renal colic and hepatic colic may all be simulated. However, the usual error is to suspect gall-stone colic. Faulkner, Marble and White have recently considered in detail the differential diagnosis of coronary occlusion and cholelithiasis. I believe the crux of the diagnostic problem is to think of the possibility of coronary occlusion, for if it be seriously considered, the evidence will usually be correctly appraised. The history is of the greatest importance, for in most instances coronary occlusion is preceded by attacks of angina or by shortness of breath on exertion. Coronary occlusion is uncommon before fifty years of age; gall-stone attacks occur frequently before. Again, coronary occlusion comes on more often in men; gall-stone colic more often in women. The feeling of constriction so characteristic of coronary disease is never experienced with gall-stone and the pain of coronary occlusion is usually more continuous. When one is prepared to place a just value upon enfeebled heart sounds, alterations of rhythm and the beginning signs of myocardial insufficiency, the careful examination of the circulatory system will usually yield distinctive evidence. It is only fair to point, as Willius has done, to the frequency with which autopsy discloses latent gall-stones after the fifth decade is passed. It must occasionally happen that a patient subject to seizures of angina will have an attack of gall-stone colic. All one can say is that the distinction between coronary occlusion and abdominal disease can usually

[7] For instances see Jones-Evans, Kalyanvala.

be made with ease, that occasionally the distinction may be difficult, and that no doubt now and again the most experienced physician will slip into error. The following instance illustrates again how difficult the distinction may be.[8]

A. L., male, white, married, aged 44 years, Laboratory janitor. Entered the Johns Hopkins Hospital (Surgical Number 65,450) February 11, 1925. Discharged April 1, 1925. The patient had always been well except for an attack of pneumonia twenty years before. There had never been any symptoms referable to the cardiovascular system. On February the 10th he worked at the hospital as usual and felt well all day and upon retiring for the night. At five o'clock the following morning he was awakened by severe pain in the epigastrium. Thinking the pain might be caused by indigestion he took soda after which he vomited. He describes the pain as being very severe, radiating up to the clavicles but not to either arm. There was also dyspnea. When seen by the Hospital externe, five hours after the onset of pain, he was extremely uncomfortable, pale, cyanotic, sweating. The temperature was 100.5°; the pulse 120, regular. Upon the assumption that the symptoms were due to some acute abdominal disease he was admitted at once to the surgical service of the Hospital. Here he was seen not only by the resident staff but by an experienced visiting surgeon and physician as well. The patient was evidently in great distress, pale, sweating, somewhat cyanotic. Lungs clear except for moist râles at both bases. Heart not enlarged, sounds clear. Pulse rapid, regular. Abdomen extremely rigid, board-like. Tenderness in the epigastrium. Leucocytes 12,240. An x-ray of the chest showed areas of consolidation at the left base, interpreted to indicate broncho-pneumonia. The diagnostic impression was that the patient had a ruptured gastric ulcer. He was operated upon shortly after admission but nothing abnormal was found in the abdomen. Subsequent course: After the operation the patient was very uncomfortable, complaining bitterly of abdominal pain. Twenty-six hours after the onset of his illness a definite pericardial friction was heard which lasted for eight hours. Forty-eight hours after the onset of his illness he had an attack of auricular fibrillation lasting ten hours. The severe symptoms soon subsided and he gradually recovered, complaining from time to time of precordial pain. The temperature on the day of admission varied from 100° to 101°; on the second day from 100° to 101.6°; on the third day from 98.6° to 100°; on the fourth day from 97.4° to 99°. Thereafter the temperature was a little elevated each day for ten days. The leucocytes on admission were 12,240; on the second day 22,000; on the third day 10,500; on the fourth day 7,000. The Wassermann reaction on the blood serum was negative. It was later thought that the clouding at the base of the left lung

[8] For similar instances see: Hardt; Ramond and Baudquin; Leon and Pollet; Engelhardt.

shown in the x-ray was probably due to pulmonary infarction. The patient left the hospital, April 1, 1925, in good condition.

THE LATE RESULTS OF CORONARY OCCLUSION

The clinical picture of coronary occlusion would be left incomplete were I to omit a word of reference to the late results of the accident. As the infarcted heart muscle is digested and absorbed, it is replaced by scar tissue and as happens in other locations lime salts are often deposited. If the area of scarring be large it forms an aneurysmal bulging which may gradually become larger and larger. In many instances the heart continues to carry on its work without noticeable impairment. The patient may die of some other cause and the unsuspected condition of the heart be revealed at autopsy. However, if the patient lives on, severe symptoms of myocardial insufficiency finally develop or else he dies suddenly from rupture of the heart. Although cardiac aneurysm is not invariably the result of coronary occlusion, still it is directly caused by it in all but exceptional instances. Since the anterior descending branch of the left coronary artery is the vessel usually plugged, aneurysm of the heart is almost always located at the apex of the left ventricle. Adhesions generally bind it to the diaphragm or the chest wall. Sternberg, in 1912, was the first to draw a well defined clinical picture by which aneurysm of the heart may be recognized. He describes four stages—First, the anginal seizure; second, the pericarditis episteno-cardica; third, a latent period free from symptoms; fourth, the development of myocardial insufficiency or sudden death from rupture. Sternberg puts altogether too much stress upon the pericarditis episteno-cardica, otherwise his description is clear and satisfactory.[9]

TREATMENT

In concluding I must justify the statement that the diagnosis of coronary occlusion has something more than academic interest, since prompt recognition of the accident may promote recovery. Although it will be impossible to verify this statement with convincing facts,

[9] For a fuller consideration of cardiac aneurysm consult Kraus, Lutembacher, Kahn; Libman's discussion, Fischer, Bourland, Fontan and Bourdon, Wilson, Christian, Ramond and Baudquin, Sezary and Alibert, Wooley, Youmans.

still experience lends it strong support. All of our clinical observations upon patients with diseased heart muscle teach us clearly that rest is a potent therapeutic measure and that strain has a damaging effect. The value of prolonged rest to a heart impaired by infections, for instance by rheumatic fever, can scarcely be questioned. In coronary occlusion the immediate outcome of the accident may depend upon getting the patient promptly at rest, and the degree to which the heart will finally regain its functional capacity may depend upon the length of time rest is enforced. Therefore, I believe it is true that in some instances the fate of the patient may depend upon the recognition of the accident. After the immediate danger is over and alarming symptoms have passed, prolonged rest insures the best possible functional restitution. When the patient feels well he wants to be up and begin to get about. If the physician has clearly in mind the character and extent of the injury the heart has suffered, he will not be cajoled into yielding to the patient's natural desires. Every week through which rest can be prolonged will improve the final functional result.

To relieve the symptoms of the attack, morphia should be given in large doses. At the same time the patient should be promptly and fully digitalized. If digitalis has not been previously given, the appropriate dose of an efficient preparation should be calculated and administered according to Eggleston's method. Not only is the digitalized heart better prepared to withstand the added burden of certain arrhythmias, should they come on, but it is also stimulated to put forth its best efforts. How desirable the best efforts may be, when a large area of heart muscle is infarcted, needs no further comment.

Note: After this paper had gone to press, Dr. Alfred M. Wedd called my attention to the valuable article of von Leyden which I had overlooked (Ueber die Sclerose der Coronar-Arterien und die davon abhängigen Krankheitszustände, *Zeitschrift f. klinische Medicin*, 1884, vii, 459). Von Leyden gives a good review of the previous literature and an excellent account of the symptoms of coronary occlusion.

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A CONSIDERATION OF ARTERIOSCLEROSIS OF THE CEREBRAL VESSELS AND THE PATHOGENESIS OF HYPERTENSION

A Preliminary Report[1]

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Anrep and Starling, in a recent study, seem to have established as a definite physiological law a fact which has long been recognized by physiologists—that a reduction in the amount of blood reaching the brain (presumably that particular part of it which has to do with vasomotor control) brings about a compensatory rise in the systemic arterial pressure. In consideration of this fact we have investigated twenty-four cases of generalized arteriosclerosis, in fourteen of which there was a definite arterial hypertension and in ten a normal or low arterial pressure. It was our purpose to determine if there were any contrasting anatomical conditions in the arterial supply of the medulla oblongata in these two types of cases. Our series is small because we have been careful to include only those cases in which clinical histories clearly established the past state of the blood pressure, realizing that such occurrences as cerebral haemorrhage, myocardial failure and other terminal events frequently bring about profound alterations in this level. Arteriolosclerosis in the medulla oblongata has been found without exception in the cases with a history of hypertension. In the cases with normal blood pressure the arterioles in this region have been found unaltered. We are now gradually increasing our series, and although at the present time it is not a large one, we feel that we are justified in arriving at the conclusion that there is at least an association between persistent hypertension and arteriolosclerosis of the vessels supplying the brain stem. In so far as it has long been recognized that arterial hypertension is accompanied by arteriolosclerosis in at least some portion of the body we suggest that a localization

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of this process in the medulla oblongata may be the essential factor in the production of persistent high blood pressure, although we recognize the objection that these changes may be secondary to the hypertension. The material upon which these conclusions have been based, together with a general discussion of our investigations, will shortly be published in detail.

BOOK REVIEWS

Lectures on Nutrition. Mayo Foundation Lectures. 243 pp. $2.50. (*W. B. Saunders and Co., Phila., 1925.*)

This series includes six lectures on the various aspects of nutrition: The measurement and significance of basal metabolism, by F. G. Benedict; Problems of metabolism, by Graham Lusk; The proportions in which proteins, fat and carbohydrate are metabolized in disease, by E. F. Du Bois; Muscular activity and carbohydrate metabolism, by A. V. Hill; Our present knowledge of vitamins, by E. V. McCollum; The relation between fertility and nutrition, by H. M. Evans.

These lectures are up to the standards which we should expect of so eminent a group of scientists. Because of the great volume of current literature which is now appearing on every phase of the subject of nutrition it is becoming increasingly difficult even for investigators, much less for those but generally interested in the subject, to keep informed of progress. In recent years there has been an increasing tendency to aid students through the publication of monographs on special subjects. In several centers of learning lecture series are now maintained, and the lectures are preserved in annual volumes. These serve a purpose similar to that of the monograph and are of the greatest importance. The Mayo Foundation is to be congratulated on publishing this series.

N. S.

Insects and Disease of Man. By CARROLL FOX, M.D. xii + 349 pp. $4.00. (*P. Blakiston's Son & Co., Phila., 1925.*)

This book is intended to serve both as a class-room and laboratory text on Medical Entomology and as a pocket manual for the use of sanitarians in the field. It is particularly adapted for use by workers in the United States, but also contains much material of value to those in foreign countries.

Part I deals with the identification, structure, habits and life-histories of the disease-carrying forms among the flies, fleas, lice, bugs, roaches, ticks and mites, while Part II treats of a long list of insect-borne diseases and of the measures that are used in their control.

Of course, much space is devoted to keys for the identification of the various disease-carrying arthropods. On the whole, these keys are very good ones, most of them being copied or adapted from the publications of recognized authorities on the different groups. Dr. Fox himself is not only a Surgeon in the U. S. Public Health Service, but also a well-known and enthusiastic student of the Siphonaptera, a fact which probably explains the presence of a ten-page key to the genera of fleas of the world—a splendid piece of work in itself, but decidedly out of place in a book of this type.

Of the 92 illustrations, 68 are from original drawings by Mr. L. H. Wilder of the Hygienic Laboratory, and are most excellent. The rest are copied from books by Stitt and others, and are not so remarkable.

The worst feature of the book is its lack of polish. There are far too many obvious typographical errors, and in some cases the keys have not been "adapted" to make their nomenclature correspond to that of the text. Then too, the figures copied from Stitt have been taken over, legends and all, word for word, without correction of certain glaring discrepancies in nomenclature or even actual errors in labelling.

But, in spite of these minor defects, this book is the best of its type yet published in this country, and may be strongly recommended, both to students and teachers of Medical Entomology and to the physician or sanitarian interested in insect-borne diseases and their control.

F. M. R.

Applied Biochemistry. By WITHROW MORSE, PH.D., Professor of Physiological Chemistry and Toxicology, Jefferson Medical College, Philadelphia. Octavo of 958 pages with 257 illustrations. $7.00. (*Phila. and London: W. B. Saunders Company, 1925.*)

The purpose of this book as stated in its preface is to "weave the woof of biochemistry into the warp of medicine." Chemical principles which have found a practical application in medicine are briefly described, and their applications given. The book is written simply and will be read with profit by those who desire a general survey of the field. Photographs of the more prominent American biochemists and brief biographical notes of the authors quoted give the book a personal touch. The vastness of the field covered makes impossible anything but a very cursory treatment of the theoretical subject matter of chemistry in medicine.

A. G.

Post-Mortem Appearances. By JOAN M. ROSS. 216 pp. $2.50. (*Oxford University Press, London, 1925*).

The author has written a handbook for pathologists. It is prepared chiefly for practitioners whose knowledge of pathological anatomy needs jogging in the event of an occasional necropsy. The information offered is for the most part correct, but for one lacking in experience it might be somewhat difficult to separate the wheat from the chaff. For example, a great deal of space is devoted to the external appearance of the body and to the contents and condition of the ventricles of the heart, details which are only occasionally important but which tend to obscure the picture and dwarf the essential lesions upon which a correct diagnosis is based. The practitioner may find it of value; students who desire a quick review of the subject could use it without harm, but as a contribution to pathology not much can be said in its favor.

J. H. B.

A Text-Book of Medical Diagnosis. By JAMES M. ANDERS, M.D., PH.D., L.L.D., and L. NAPOLEON BOSTON, A.M., M.D. Third edition, entirely reset with 555 illustrations, 21 in colors. 1422 pp. $12.00. (*W. B. Saunders Company.*)

This stupendous text-book, of 1422 pages, contains an encyclopaedic amount of knowledge. History taking, anatomy, physiology, pharmacology, physical diagnosis, neurology, clinical microscopy, radiography, electrocardiography, and indeed all clinical and physical methods of investigation are taken up, sometimes at a length which might embarrass the student who is seeking information to help him in making a diagnosis in a specific case. Hence, the work would seem preferable as a book of reference than as a text-book.

E. W. B.

A Text-Book of Chemistry and Chemical Uranalysis for Nurses. By HAROLD L. AMOSS, M.D. 248 pp. $2.25. (*Lea and Febiger, Phila. and New York, 1925.*)

This is the third edition of Dr. Amoss's valuable little compendium of chemistry for nurses—for nurses, because it takes for granted some previous knowledge of the subject and contains pertinent remarks upon the chemistry of certain substances of importance in medicine. Moreover, there is a minimum of attention to laboratory experimentation; the author assumes that laboratory demonstrations shall be given by the instructor, while the student's attention is to be directed to the understanding of chemical principles. This seems to us a very wise division of labor. An exception to the rule is found in the chapter on Uranalysis, where ample directions for laboratory tests are found. Some understanding of chemical formulae is about the only preliminary knowledge required in approaching the book: the principles involved, however, could be grasped by any intelligent student without preliminary training.

The third edition contains a sensible exposition of the subject of hydrogen-ion concentration. On the whole, it seems to us that this book should have a wide field of usefulness and that it deserves many more editions.

J. T. K.

Diet in Health and Disease. By J. FRIEDENWALD AND J. RUHRÄH. Sixth Edition. 987 pp. $8.00. (*W. B. Saunders Co., Phila. and London, 1925.*)

This book has just been thoroughly revised by the authors who offer a compendium of diet lists and dietary therapeutic principles that is remarkably complete. It is a large book, and is useful rather as a reference work from which dietaries may be obtained than as a book to be read by the student to obtain principles of treatment by diet. The reasons for the use of certain diets are perhaps not so freely given as the diets themselves, though the usefulness of the diets in the conditions toward which they are directed is not to be questioned. The volume is one that will prove very useful to the busy practitioner.

J. T. K.

Tumors of the Colon and Rectum. Their Pathology, Diagnosis and Treatment. By JEROME M. LYNCH, M.D. Surgical Director, St. Bartholomew's Hospital, N. Y., and JOSEPH FELSEN, M.D. Attending Pathologist, St. Bartholomew's Hospital, N. Y. 259 pp. $12.00. (*Paul B. Hoeber, New York, 1925.*)

This monograph presents the important facts about new growths in the large bowel from both the clinical and pathological points of view. It is unusually well illustrated with excellent cuts, and a feature of its arrangement is the grouping of illustrations of specimens on one page with the clinical data bearing upon the same case on the page facing. This makes a vey convenient arrangement for the quick presentation of all the facts bearing on that particular case. The book is well gotten up as to type, appearance and other physical qualities. There is an extensive bibliography and a good index. A few minor points of criticism are as follows: there are several errors of proof reading as exemplified in the legends under some of the illustrations; the use of "prone" for "supine" on page 168 and of "suture" for "surface" on page 175. Again, in spite of the extensive bibliography, we find no mention of the names of several eminent contributors to the subject, notably, Dan Jones, Miles and Coffee. The student will find very little in the book that is really new. Regarded, however, as a collection and presentation of our present day knowledge, it is entirely acceptable and will serve as a very useful work of reference.

H. B. S.

The Development of Psychoanalysis. By S. FERENCZI and OTTO RANK. 68 pp. $2.00. (*Nervous & Mental Disease Publishing Co., New York and Washington, 1925.*)

This book is a brief résumé of the growth of psychoanalysis. It presupposes in its readers a certain amount of technical knowledge of the subject. It presents nothing new but gives in concise form the salient changes in the analytic technique and theory with special emphasis on the Freudian School.

Chapter II—The Analytic Situation—and Chapter III—A Historical Critical Retrospect—contain the most important material. In Chapter II the analytic method and its theory are explained. In Chapter III the evolution of the theory and technique are discussed, with a criticism of the difficulties which came up at the various stages.

C. M. T.